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FISCAL YEAR 1983⁸²

(1 October ¹⁹⁸¹1982 - 30 September ¹⁹⁸²1983)

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UNITED STATES ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER WASHINGTON, D.C., 20307

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UNITED STATES ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5300

ANNUAL REPORT
(1 October 1981-30 September 1982)

Thomas P. Sweeney, COL, DC

October 1982

Supported by

US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) DA Project 3M161102BS10 Management of Dental Injury and Combat Dentistry. Task DA The objectives are to obtain information by the techniques of clinical and basic research on injuries and diseases, except communicable diseases, commonly seen in soldiers, especially in field operations and overseas. The work is divided according to the major dental specialties. Emphasis is placed on diseases and injuries that are receiving little or no study by civilian.		

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Item 19 continued:

Emergencies; Dental X-ray; Diphosphoinositide-Lysozyme; Gentamicin; Gingival Exudates; Granular Tricalcium Phosphate; Herpetic Lesions; High Velocity Missile Effects; Impression Materials; Infection Control; Inhibition of Bone Resorption; Investment Techniques; Laboratory Animals; Lidocaine; Lip Pathology; Lymphocytes; Marginal Leakage; Maxillofacial Wounds; Microencapsulated Antibiotics; Monoclonal Antibodies; Nerve Agent; Oral Health Status; Polymer Devices; Porcelain-Metal Bond; Post and Core Restorations; Prostaglandin; Radionuclide X-ray System; Recurrent Aphthous Stomatitis; Reinforced Resin; Resin Restorative; Salivary Amylase; Salivary Enzyme; Salivary Physiology; Secondary Missiles; Segmental Mandibular Defects; Soldering Base Metals; Sporicidin; Storage Stability; Subtraction Radiography; Sustained Release Antibiotic; Tracheal Grafts; Tricalcium Phosphate; Wound Healing; Xerocheiliosis.

Item 20 continued:

research groups, and the work is aimed at providing better preventive measures as well as treatment.

DA Project 3S162775A825 Combat Maxillofacial Injury.
Tasks AA, AB

The objectives are to develop simplified procedures for the care of complex maxillofacial wounds and injuries which require long time-consuming procedures for reconstruction; to achieve minimal morbidity rates from oral emergencies, preventable oral disease, and restorative failures; and to develop more efficient, simplified, effective clinical and laboratory techniques which will result in better utilization of manpower and a saving in time and materiel.

DA Project 3M162734A875 Medical Defense Against Chemical Agents.
Task AQ

The objectives and purposes are the development of the basic scientific data required for systems of soldier CW agent antidotes, soldier/patient decontamination, and medical management of CW casualties.

Military

FOREWORD

IN CONDUCTING THE RESEARCH DESCRIBED IN THIS REPORT, THE INVESTIGATORS ADHERED TO THE "GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS" AS PREPARED BY THE COMMITTEE ON CARE AND USE OF LABORATORY ANIMALS OF THE INSTITUTE OF LABORATORY ANIMAL RESOURCES, NATIONAL RESEARCH COUNCIL.

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TELEPHONE: ^a 202-576-3484				TELEPHONE: ^a 202-576-3764			
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Foreign Intelligence Considered				ASSOCIATE INVESTIGATORS			
				NAME: ^a Woodward, S., COL, DC			
				NAME: ^a Heath, J., M.S., Miller, R., B.S.			
				NAME: ^a Wynkoop, J., CPT, DC			
22. KEYWORDS (Precede EACH with Security Classification Code) ^a (U)Diphosphoinositide-Lysozyme (U)Citric Acid (U)Prosta- glandin (U)Copolymer (U)Inhibition of Bone Resorption (U)Cyclic AMP (U)Laboratory Animal							
23. (U) Recent studies show that 10-12% of combat wounds involved the maxillofacial apparatus. Further, 7% of noncombat injuries requiring hospital care involve the maxillofacial region. This results in the loss of approximately 1,000,000 man-hours per year. The research objective is to accelerate or otherwise improve the healing of maxillofacial injuries.							
24. (U) Studies on the effects of biochemical and physical factors to include chelate complexes, cyclic AMP, prostaglandins, and <i>in vivo</i> growth factors on the rate of healing in soft tissue and bone will be done. The mechanism of any beneficial alteration in healing effected will be invested and pursued to human usage.							
25. (U) (81 10 - 82 10) A diphosphoinositide-lysozyme (DPIL) complex was found to accelerate the healing of osseous wounds in rats as did a combination of polylactic (PLA) and polyglycolic (PGA) acid (50:50). Combined-DPIL and 50:50 PLA-PGA was also evaluated in the same system. Available data indicate a greater acceleration of osseous healing with combined DPIL-copolymer than with either alone. Data collection is continuing. Combined PLA-PGA with Dilantin did not accelerate osseous healing. Studies on the effects of PGE ₂ and cyclic nucleotides on osseous and pulpal healing are also in progress. Citric acid was found of value in accelerating the healing of gingival tissues. Efforts continue to isolate a powerful inhibitor of bone resorption. A 50% inhibition ⁴⁵ Ca release from fetal long bones has been obtained. The nature and mode of action of this inhibitor remain to be determined.							

^aReliable to contractors upon originator's approval.

DD FORM 1498

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PROJECT: 3M161102BS10
WORK UNIT TITLE: ACCELERATION OF WOUND HEALING
PRINCIPAL
INVESTIGATOR: LTC JEFFREY O. HOLLINGER, DC

A Study on the Behavior of Bone in Organ Culture With
Special Emphasis on PGE₂ and Indomethacin

PROBLEM: There is abundant clinical and experimental evidence that bone can synthesize PGE₂, and that local synthesis of this prostaglandin leads to local bone resorption. It is believed that PGE₂ causes an increase in the number of osteoclasts and heightens their lytic activity. Combat injury can produce mechanical stress to periosteum, causing perturbation of the tenant cell membranes with a resultant increase in the synthesis and release of prostaglandins of the E series. Surgical treatment and healing of osseous wounds would have a more predictable and reliable incidence of repair if the endogenous prostaglandin E series of lytic agents could be thwarted. Indomethacin has generated considerable attention due to its remarkable ability to inhibit PGE₁ and PGE₂ synthesis. If indomethacin could effectively inhibit PGE₂ synthesis by bone in vitro, this would be the first step to better understand PGE₂ and a potential in vivo inhibitor.

APPROACH: A total of 192 calvaria from D/O neonatal CD-1 mice were aseptically removed and placed in plastic media dishes - one calvaria per dish. The dishes were gassed with a mixture of 5% CO₂ and air. The calvaria were divided into four treatment groups: (1) Control: no exogenous agents; (2) Indomethacin: 200 ng/ml of medium; (3) PGE₂: 100 ng/ml of medium; and (4) Combination: 100 ng/ml PGE₂ plus 200 ng/ml indomethacin. Calvaria were harvested at 24, 48, and 72 hours and were processed for histomorphometric evaluation, radioimmune assays of PGE₂ and cyclic GMP and AMP, and for atomic absorption spectrophotometry for calcium and phosphate molar ratios.

RESULTS AND DISCUSSION: Assays have not yet been finished. The histomorphometry analyses have been completed and do not support the findings of Holtrop, Raisz, and King - that PGE₂ stimulates pre-existing osteoclastic activity. Rather, PGE₂ increased the number of osteoclasts - a finding similar to Schelling, Wolfe, and Tashjon. Also, indomethacin added to control dishes inhibited spontaneous basal bone resorption. Indomethacin had no effect on calvaria osteoclasts in dishes when exogenous PGE₂ was added to the medium. Further studies are under way to evaluate PGE series inhibitors; these include: ficose-5,8,11,14 tetraynoic acid, 5-oxa and 7-oxa-pyrostanoate derivatives, linolenic acid, phenylbutazone, and dichloromethane diphosphonate.

PROJECT: 3M161102BS10
WORK UNIT TITLE: ACCELERATION OF WOUND HEALING
PRINCIPAL
INVESTIGATOR: LTC JEFFREY O. HOLLINGER, DC

Enhanced Healing of Soft Tissue Wounds Using Diphenylhydantoin

Sodium Incorporated Into a Meshwork of Biodegradable

Copolymer (50:50 Poly L-(-)Lactide-co-Glycolide)

PROBLEM: High velocity projectiles from military weapons produce a wide variety of tissue destruction. Frequently, significant amounts of soft tissue are avulsed. These sites often require extensive skin grafting. Unfortunately, bulk replacement material for the connective tissue bed is scarce. The resultant healing site is "cupped-out," concave, and grossly unesthetic. A material that is biocompatible and that can induce collagen formation to "bulk-up" the connective tissue bed will insure for an esthetic effect. In addition, if the material can hasten collagen formation in the wound site, this may prove to be an important aid in facilitating the healing of surgical and traumatic wounds.

APPROACH: The copolymer of 50:50 poly L-(-) lactide-co-glycolide was solubilized in methylene chloride and diphenylhydantoin was added, and using nitrogen, a fibrous mesh dressing was prepared. The dressing was placed onto surgical wounds created on the backs of rats. Healing was compared to plain copolymer, untreated, and IP-diphenylhydantoin-sodium treated wounds. Wounds were evaluated by assaying for total protein hydroxyproline; using RIA for Dilantin released in the animal; by tensile testing; and by histomorphometry.

RESULTS AND DISCUSSION: After 28 days there was no significant difference in the rate of healing between any of the four treatment groups. However, animals that were receiving the IP-diphenylhydantoin-sodium did display a greater amount of collagen and a higher density of fibroblasts than the other three treatment groups. It was also apparent that the physical properties of the copolymer dressing were not as favorable as had been anticipated. By 3 days, most dressing material had become brittle and had begun to fray. Therefore, it could not be closely apposed to the healing connective tissue bed. Consequently, the release of diphenylhydantoin-sodium into the healing sites was inadequate. A supple, cellophane-type copolymer dressing was prepared and evaluated to militate against such a problem.

PROJECT: 3M161102BS10

WORK UNIT TITLE: ACCELERATION OF WOUND HEALING

PRINCIPAL
INVESTIGATOR: LTC JEFFREY O. HOLLINGER, DC

A Study on 50:50 PLA:PGA+DPI-L for the Promotion of Calcification
in Osseous Defects

PROBLEM: Approximately 10% of combat injuries are in the maxillo-mandibulo-facial region. For a casualty of this type, establishment of structural and anatomical continuity is an extremely important goal in the early management and restoration of function. Current treatment of avulsive and fracture wounds of the maxillo-mandibulofacial region includes a variety of implant materials (autografts, allografts, xenografts) and an array of metallic fixation devices. Some materials may initiate an adverse immune response. Most metallic fixation devices eventually require surgical removal. Both situations are unacceptable. If a biocompatible, biodegradable implant could be developed, then adverse host reactions would not occur and surgical removal would not be required.

APPROACH: In an attempt to develop a biocompatible, biodegradable implant material that could initiate osseous healing, copolymers of polylactic and polyglycolic acids in combination with an acidic phospholipid-lysozyme complex were evaluated. Each component of the implant material was examined for host acceptability and bone inductive effects. Endochondral and intramembranous bone defects were treated in experimental animals. In separate experiment the acidic phospholipid-lysozyme complex and the PLA:PGA (in a 50:50 ratio) were individually assessed at the host sites in the following ways: histomorphometrically, histochemically, by enzyme analyses, by total protein and hydroxyproline assays, and by elemental analyses. After the data analyses for these experiments, the combination of copolymer (50:50 PLA:PGA) and acidic phospholipid-lysozyme was evaluated in a similar fashion.

RESULTS: In experimental animals, the acidic phospholipid-lysozyme complex induced healing of osseous wounds at a more accelerated tempo than wounds receiving no treatment. In a separate experiment, at 7, 14, 21, and 28 days the copolymer treated bony wounds had healed more rapidly than untreated wounds. By 42 days, the rate of healing was similar between the treated and untreated groups. All phases of the evaluation of the combination type implant have not yet been completed. The currently available data indicate that the copolymer-acidic phospholipid-lysozyme complex does induce calcification at a more rapid rate than the untreated or single reagent treated osseous wound.

PROJECT: 3M161102BS10

WORK UNIT TITLE: ACCELERATION OF WOUND HEALING

PRINCIPAL

INVESTIGATOR: LTC JEFFREY O. HOLLINGER, DC

A Study of Prostaglandins and Cyclic Nucleotides

and Their Reaction to Pulpal and Periapical Pain

PROBLEM: Prostaglandins are one of the most prevalent of the autacoids. Their synthesis is orchestrated by astonishingly diverse stimuli. The prostaglandins produce a remarkably diverse spectrum of effects, one of which is as a mediator for pain. Pain is one of the most singularly insidious modalities responsible for eroding both cognitive and actively dexterous skills. Cephalic pain, and specifically toothache pain, are profound stress inducers that create havoc with the soldier's psyche. By isolating and identifying pain mediating biochemicals endogenous to pathological pulpal and periapical tissues, it may be possible to militate against their synthesis, thereby obliterating certain types of dental pain. Elimination or modification of pain will help to insure for a soldier's high performance in activities that require recognition and dexterity.

APPROACH: Tissue samples will be retrieved from four sources, with at least fifteen specimens from each source. There will be four categories of sources: (1) Vital asymptomatic pulp; (2) Vital symptomatic pulp; (3) Asymptomatic periapical lesions; and (4) Symptomatic periapical lesions. After removal, all tissues will be immersed immediately in LN₂ or dry ice and will be stored at -40C until needed. Assays will consist of RIA's for PGE₁, PGE₂, PGF_{2d}, cAMP, and cGMP.

RESULTS: The study is at the tissue collection stage. Assays have not yet begun.

PROJECT: 3M161102BS10

WORK UNIT TITLE: ACCELERATION OF WOUND HEALING

PRINCIPAL
INVESTIGATOR: COL STEPHEN G. WOODYARD, DC

Evaluation of Citric Acid Enhancement of Oral Soft Tissue

Healing on Previously Denuded Tooth Root Surfaces

PROBLEM: Early return of the injured soldier to duty is of paramount importance, placing an emphasis upon methods and techniques which can accelerate wound healing in the maxillofacial area. Contamination of tooth surfaces, soft tissues, and bone subsequent to wounding in the oral region occurs routinely due to the presence of saliva and oral microorganisms in that area, complicating the healing process. Of particular importance are root surfaces of teeth partially avulsed or exposed by loss of adjacent soft tissues and bone, contamination resulting in delay and prevention of healing of soft tissues and bone placed adjacent to these surfaces during subsequent surgical repair. Mechanical debridement of contaminated tooth surfaces prior to coverage with soft tissues and bone is relatively ineffective, often resulting in subsequent loss of such teeth. Studies comparing mechanical debridement to a combination of such treatment and lavage with citric acid indicated acceleration of wound healing occurs in uncontaminated oral wounds involving tooth surfaces, but little data exists relative to its usefulness in contaminated wounds.

APPROACH: Six cynomolgus monkeys had facial root surfaces surgically exposed by removal and repositioning of soft tissues and bone. Six weeks of exposure and contamination of tooth surfaces by saliva, oral microorganisms, and their products followed prior to surgical repair. Tooth surfaces were treated by either mechanical debridement alone or in combination with topically applied pH 1.0 citric acid for 3 minutes. Soft tissues were placed over treated root surfaces and animals were sacrificed at varied time intervals up to 42 days postsurgical repair. Areas including treated teeth, soft tissues, and bone were removed, fixed, and prepared for histologic and biometric evaluation.

RESULTS: All areas treated with both mechanical debridement and citric acid healed rapidly with new connective tissue attachment, much as existed prior to creation of the wounds. Conversely, mechanical debridement alone resulted in incomplete repair with an epithelial interface between soft tissues and tooth surfaces. No adverse soft tissue or bone responses occurred subsequent to citric acid application. Study indicates use of citric acid following conventional mechanical debridement of contaminated root surfaces is advisable, resulting in both acceleration of soft tissue healing and improvement of the final healing result.

PROJECT: 3M161102BS10

WORK UNIT TITLE: ACCELERATION OF WOUND HEALING

PRINCIPAL
INVESTIGATOR: JAMES R. HEATH, III

Identification of Leukocyte Populations Responsible for Production
of OAF and Their Role in Bone Resorption

PROBLEM: There is a retardation of osseous repair in wounds that become infected, a common occurrence in traumatic combat injuries - especially those of the maxillofacial apparatus. One of the factors thought to be responsible for this delayed healing is the lymphokine osteoclast activating factor (OAF). OAF is produced by lymphocytes in response to stimulation by bacterial products and results in activation of local osteoclasts which in turn leads to enhanced bone resorption and retardation of osseous repair. OAF has also been implicated in the osseous deterioration seen in periodontal disease and in multiple myeloma patients. An investigation into the mechanism of production and modes of action could lead to abrogation of the detrimental effect of OAF and thus a quicker return of the soldier to duty.

APPROACH: OAF is produced by stimulating human lymphocytes with the mitogen phytohemagglutinin in large volume cell culture. The nanogram quantities of OAF in the cell culture supernatants are concentrated and partially purified by an ultrafiltration protocol developed in our laboratory. Further purification is accomplished by a variety of techniques including ammonium sulfate precipitation, gel filtration, ion exchange chromatography, high performance liquid chromatography, and polyacrylamide electrophoresis. Osteolytic activity (OAF) is detected in culture supernatants and purified fractions by a bioassay system involving the release of ^{45}Ca from fetal rat long bones in organ culture.

RESULTS: Osteolytic activity has been found in cell culture supernatants and in gel filtration fractions representing a variety of molecular weights from 18,000 to approximately 1,500 as estimated by gel filtration. These results agree with those of others suggesting that OAF exists in a system of freely associating-disassociating active sub-units. The amount of disassociation increases with increasing ionic strength of the medium. An unexpected discovery was the presence of an apparent powerful osteolytic inhibitor in the lymphocytes culture supernatants, reported in FY 80-81. The presence of this inhibitor has been confirmed in all subsequent culture supernatants and its molecular weight is estimated to be slightly less than 6,000. This inhibitor has been further purified and results in greater than 50% inhibition of ^{45}Ca release from fetal rat long bones in the bioassay system. More work is needed to determine the nature and mode of action of this inhibitor and its possible role in vivo.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)6J6	
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10. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER		
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B. CONTRIBUTING							
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				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
21. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Vincent, J., LTC, DC Miller, R., B.S.			
				NAME: Wynkoop, J., CPT, DC Heath, J., M.S.			
22. KEYWORDS (Precede EACH with Security Classification Code) ^a (U) Microencapsulated Antibiotics; (U) Infection Control; (U) Wound Healing; (U) Sustained Release Antibiotic; (U) Laboratory Animals							
23. (U) To evaluate the special military problems of drug storage, heat susceptibility, long-term drug potency, sterility of bulk items, lack of refrigeration in combat zones and delivery to the patient. To investigate drug hazards. To investigate the use of biodegradable polymers for the long-term, slow release of drugs.							
24. (U) Improved means of drug delivery in the field using microencapsulated medicaments will be studied. The hazards in the use of various drugs and the use of biodegradable, biocompatible materials for surgical repair of combat wounds will be studied.							
25. (U) (81 10 - 82 10) Although as previously reported microcapsules made of 68:32 DL-PLGA effectively eliminated wound infections in rats, they biodegraded too slowly and released drug for too long a time. Most recently, microcapsules have been polymerized from a 50:50 DL-PLGA excipient using a better polymerization catalyst and purer monomers. These microcapsules met the target duration of release of 14 days and are presently undergoing <i>in vivo</i> evaluation. Gentamicin sulfate microcapsules prepared from 68:32 DL-PLGA dumped drugs too rapidly and failed to eliminate infection in the infectious rodent model. A more extensive development program will be required to solve problems inherent in encapsulating this drug.							

^a Available to contractors upon originator's approval.

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1 MAR 68

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AND 1498-1 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

PROJECT: 3M161102BS10

WORK UNIT TITLE: THE PROBLEMS INVOLVED IN MILITARY ORAL HEALTH CARE
DELIVERY RELATED TO THERAPEUTIC AGENTS AND MATERIALS

PRINCIPAL
INVESTIGATOR: JEAN A. SETTERSTROM, PHD

Biological Activity Verification of Specified

Microencapsulated Antibiotics In Vivo

PROBLEMS: Combat wounds are characterized by a high incidence of infection primarily because of the inevitable presence of devitalized tissue and foreign body contaminants from missile fragments that carry dirt and debris into the wound. During evacuation, the wound may be exposed to further contamination and delay before initial treatment. Wound healing in the combat casualty, therefore, must overcome adversities not seen in the highway victim or civilian counterpart. Among soldiers, infections have remained a major cause of morbidity that results in lengthened hospitalization and combat ineffectiveness.

APPROACH: Improved methods to deliver antibiotics to contaminated tissue following traumatic injury are needed in order that sustained and effective tissue levels of antibiotics can be maintained at the wound site in spite of the inadequate perfusion of blood resulting from shock or the destruction of blood vessels to devitalized areas. The improved method should be easily applied in a single dose to the wound site as soon as possible after injury when infection is most likely to be suppressed. Such a novel antibiotic delivery system is being developed in which ampicillin anhydrate and gentamicin sulfate are being incorporated individually into microspheres of biocompatible, biodegradable, copolymer that are formulated to slowly release the drug over a sustained period (14 days). These microspheres which will completely biodegrade once all drug is released exist as a free-flowing powder that can be easily dusted onto wounds under field conditions.

RESULTS: Studies to formulate microcapsules with optimal drug release kinetics have been ongoing. Prior to this year, microcapsules were prepared from a 68:32 DL-PLA:PGA excipient that biodegraded about 30-50 days post-treatment giving an undesirably long release of drug. Most recently, microcapsules have been polymerized from a 50:50 DL-PLA:PGA excipient using a better polymerization catalyst and purer monomers. These microcapsules meet the target duration of release of 14 days. By carefully standardizing materials, methods and processes used in the design of these microcapsules, and following successful in vivo efficacy evaluations, clinical testing of the ampicillin microcapsules should be possible by 1984.

The success achieved with encapsulated ampicillin in controlling wound infections in a rodent model has stimulated interest in the encapsulation of other antibiotics. Encapsulation of additional antibiotics are desir-

able so that encapsulated mixtures can be formulated to assure broad spectrum antibiotic management for wound therapy. During this year, gentamicin sulfate microcapsules prepared with a 68:32 DL-PLA excipient were produced, however, results of in vitro and in vivo evaluations indicated that these microcapsules dumped drug too rapidly to be effective in controlling wound infections. A more extensive development program will be required to solve problems inherent in the encapsulation of this drug.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)36	
				DA OF 6024	82 10 01		
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY DCTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8. ORIGIN NOTE ^a	9. SPECIFIC DATA- CONTRACTOR ACCESS	10. LEVEL OF DOW A. WORK UNIT
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
11. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER		
A. PRIMARY	61102A	3M161102BS10		DA	363		
B. CONTRIBUTING							
C. Contributing	//////////	STOG 80-7.2:5					
12. TITLE (Provide with Security Classification Code) ^a							
(U) Identification and Control of Oral Infections							
13. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
010100 Microbiology; 002300 Biochemistry							
14. START DATE		15. ESTIMATED COMPLETION DATE		16. FUNDING AGENCY		17. PERFORMANCE METHOD	
66 07		CONT		DA		C. IN-HOUSE	
18. CONTRACT/GRANT				19. RESOURCES ESTIMATE		20. PROFESSIONAL MAN YRS	
A. DATE/EFFECTIVE:				PRECEDENCE		B. FUNDS (in thousands)	
B. NUMBER ^a				82		2.0	
C. TYPE:				FISCAL YEAR		130	
D. KIND OF AWARD:				CURRENT		154	
E. CUM. AMT.				83		2.0	
21. RESPONSIBLE DOW ORGANIZATION				22. PERFORMING ORGANIZATION			
NAME ^a USA Institute of Dental Research				NAME ^a USA Institute of Dental Research			
ADDRESS ^a Washington, DC 20012				ADDRESS ^a Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)			
NAME: SWEENEY, T.P.				NAME ^a Setterstrom, J.			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3662			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
23. GENERAL USE				ASSOCIATE INVESTIGATORS			
				NAME: Woodyard, S.			
				NAME: Vincent, J., Heath, J.			
24. KEYWORDS (Provide each with Security Classification Code) ^a (U) Oral Health Status; (U) Gingival Exudates;							
(U) Crevicular Fluid; (U) Sporocidin; (U) Cidex (U) Monoclonal Antibodies							
25. TECHNICAL OBJECTIVE, 26. APPROACH, 27. PROGRAM (Provide individual paragraphs identified by number. Provide rest of each with Security Classification Code.)							
23. (U) To investigate the source and treatment of oro-facial infections encountered in field conditions, foreign countries and diverse climates. To evaluate the special agents, instruments and chemicals necessary under military conditions.							
24. (U) Oro-facial infections of significance in the diverse military environment will be studied by microbiological, immunological, and electronmicroscopy methods. Possible sources of oral infections will be evaluated and the effectiveness of commercially available as well as in-house designs will be studied for their ability to control or prevent oral infections.							
25. (U) (81 10 - 82 10) Development of a rapid non-immune biochemical technique for evaluating oral health status based on the hydroxyproline content or gingival exudates has continued. Improved clinical collection methods and quantitative evaluation procedures have been developed and a baseline study on clinical variations is in progress. A clinical study of the relative efficacies of the cold sterilizing agents sporocidin and cidex is continuing. Thus far sporocidin has exhibited the more useful properties. A study has been initiated on the use of monoclonal antibodies for the rapid identification of anaerobic microorganisms associated with maxillofacial wound infections.							

PROJECT: 3M161102BS10

WORK UNIT TITLE: IDENTIFICATION AND CONTROL OF ORAL INFECTIONS

PRINCIPAL

INVESTIGATOR: COL STEPHEN G. WOODYARD, DC

Measurement of Collagenolytic Activity

in Areas of Chronic Infection

PROBLEM: A reliable, noninvasive means for evaluating tissue healing or degradation is needed. Current state of the art methods are not significantly better than those used during ancient times which describe tissue color, swelling, temperature, and presence or absence of hemorrhage. Invasive methods such as biopsy are of some value in certain pathologic states, but are of little use in measuring healing activity, this being a phenomenon essentially unmeasurable by visual observation of tissue sections as well as being contraindicated in healing wounds. Hydroxyproline is a product of collagen degradation, found in no other tissues other than a minor component of a serum complement fraction, suggesting variation of hydroxyproline levels would occur directly with inflammatory collagenolysis. If such levels could be correlated reliably with known levels of tissue destruction and new or established clinical indices, more reliable evaluations could be made relative to tissue healing status and the relative effectiveness of therapeutic regimens used in treatment of the wounded soldier in the field environment.

APPROACH: An area readily available for studies of chronic or acute destruction in intraoral areas is the soft tissue/tooth interface termed the gingival sulcus. Treatment of that highly contaminated area subsequent to acute infection provides an ideal model for studies on wound healing in intraoral wounds.

RESULTS: Data have been obtained that indicate that hydroxyproline levels vary directly with increased areas of clinically measured destruction. A significant step forward was taken by the development of a reliable and highly accurate method for processing collected exudates and evaluating quantitative hydroxyproline levels. Improved clinical collection methods to include improved quantitative measurements of exudate levels has been developed which will allow accurate evaluation of concentration of hydroxyproline in tissue fluids. A study is in process to determine base line levels of hydroxyproline and diurnal variation in varying states of inflammation and tissue destruction prior to evaluating effects of various therapeutic procedures.

PROJECT: 3M161102BS10

WORK UNIT TITLE: IDENTIFICATION AND CONTROL OF ORAL INFECTIONS

PRINCIPAL
INVESTIGATOR: M. A. DEREVJANIK

Evaluation of Cold Sterilants

PROBLEM: (1) To determine which glutaraldehyde-based disinfectant, Sporidicin or Cidex, is superior in efficacy and cost effectiveness, (2) to determine the dilution and duration of effectiveness for each cold sterilant during clinical use, and (3) to determine the effect of storage conditions on the stability of the constituent chemicals of each agent when subjected to temperatures equivalent to climatic extremes.

APPROACH: The cold sterilants were evaluated using the official methods of analysis of the Association of Official Analytical Chemists (AOAC) by performing the AOAC spore, bactericidal, and tuberculocidal tests. Solutions were tested at different dilutions under various conditions. These conditions included timed sampling following shelf activation in the laboratory, as well as samples removed from disinfectant trays following use in the clinic. Phase 3 of the problem will be addressed during the next year. In this phase, samples of each cold sterilant will be subjected for known time intervals to various humidities and temperatures to stimulate climatic conditions likely to be incurred under field conditions. Subsequently, the cold sterilants will be tested for efficacy.

RESULTS: Part 1 of the problem has been completed and reported on previously. Briefly, Sporidicin was found to retain an effective sporicidal activity at dilutions five times, and an effective disinfection dilution fifteen times that of Cidex. Evaluation of samples removed from disinfection trays following use for 1, 2 and 3 weeks in the dental clinic showed Sporidicin to retain sporicidal activity after 3 weeks of use. Cidex, however, failed to exhibit sporicidal activity after 2 weeks. Sporidicin, when diluted 1:5, retained the same sporicidal activity of full-strength Cidex. Bactericidal testing of clinically used disinfectant to determine the lowest concentration of each agent that is bactericidal for a 2-3 week period is ongoing.

PROJECT: 3M161102BS10

WORK UNIT TITLE: IDENTIFICATION AND CONTROL OF ORAL INFECTIONS

PRINCIPAL

INVESTIGATOR: LTC JACK W. VINCENT, DC

Production and Utilization of Monoclonal Antibodies
in the Rapid Identification of Anaerobic Microorganisms
Associated with Maxillofacial Infections

PROBLEM: There is currently no rapid method for the identification microorganisms present in a wound exudate. Conventional techniques require approximately 2 to 3 days for this procedure. Such a delay in evaluating contaminated maxillofacial wounds and in selecting appropriate antibiotic therapy could result in severe sequelae. A method of rapid detection would appear to be ideal for the prevention of such a delay and may serve as a model for the detection of biological agents which might be utilized in a biological warfare environment.

APPROACH: Mice will be immunized with selected microorganisms which are commonly associated with maxillofacial wound infections. The spleen will be harvested and cells dispersed. These lymphoid cells will be used with mouse myeloma cells in polyethylene glycol to form hybridoma cells. Efforts will be directed to isolate a clone of cells possessing immortality and secreting a monoclonal antibody specific for the microorganism of interest. When isolated, this monoclonal antibody will be used to develop a system for rapid detection (2-3 hours) of wound contaminants. Such a system (most probably the ELISA) must display extreme sensitivity and specificity which should be provided by these techniques.

RESULTS: The organisms Fusobacterium nucleatum (ATCC 20953) and Bacteroides gingivalis (ATCC 33277) have been selected and compared with clinical isolates of these organisms by polyacrylamide gel electrophoresis. They were found to be identical. Separate mice were immunized with F. nucleatum and B. gingivalis and fusions are being performed with mouse myeloma cells.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)616	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8A. DISSEM INSTR ^a	8B. SPECIFIC DATA - CONTRACTOR ACCESS ^a	9. LEVEL OF SUM ^a
81 10 01	K. COMP	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
10. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
A. PRIMARY	61102A	3M161102BS10		DA		364	
B. CONTRIBUTING							
C. CONTRIBUTING	//////////	STOG 80-7.2:5					
11. TITLE (Precede with Security Classification Code) ^a (U) The Secondary Effect of High Velocity Missiles on Cranofacial Tissues							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a 012900 Physiology							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
81 10		82 10		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
A. DATES/EFFECTIVE:				PRECEDING			
B. NUMBER: ^a				FISCAL YEAR		B. FUNDS (in thousands)	
C. TYPE:				82		0.5	
D. KIND OF AWARD:				83		0	
E. CUM. AMT.						30	
20. RESPONSIBLE DOD ORGANIZATION				20. PERFORMING ORGANIZATION			
NAME: ^a USA Institute of Dental Research				NAME: ^a USA Institute of Dental Research			
ADDRESS: ^a Washington, DC 20012				ADDRESS: ^a Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P., COL, DC				NAME: ^a Carpenter, W.M., COL, DC			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3080			
21. GENERAL USE				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
Foreign Intelligence Considered				ASSOCIATE INVESTIGATORS			
				NAME: Lewis, D., LTC, DC			
				NAME:			
22. KEYWORDS (Precede EACH with Security Classification Code) ^a (U) Cranofacial Tissues; (U) High Velocity Missile Effects (U) Maxillofacial Wounds; (U) Secondary Missiles; (U) Laboratory Animals							
23. (U) To conduct a systematic evaluation of animal tissues (eyes and brains) subjected to trauma as a result of high velocity missiles striking the maxillofacial complex. The increasing numbers and velocity of missiles produced by modern weaponry results in a significant increase in the production of tooth and bone fragments which can do extensive damage as secondary missiles remote from the primary missile impact site. The objective of this study is to provide a semi-quantitative evaluation of the secondary effects of high velocity missile impacts and to provide data for the "Computer Man" system which will help to define treatment strategies for a wide range of combat wounds.							
24. (U) Forty-five Texas Angora goats were shot in the maxillofacial complex with high velocity missiles of various sizes in a USAIDR contract project. At autopsy the eyes and brains were removed intact. Detailed histologic evaluations of these tissues will be made using conventional qualitative methods as well as new methods which will provide quantitative data.							
25. (U) (81 10 - 82 10) The eyes of 45 Texas Angora goats were prepared for histologic evaluation (H&E, PAS and Trichrome stains). The brains were examined grossly and xero-radiographically. Ten of the goats sustained fractures of the orbit and one had hemorrhage in the viterious body. Four of the brains had gross focal hemorrhage. No gross or microscopic bone or tooth fragments were found in the brain or eyes. Because of their anatomic configurations the goats sustained minimal damage to eyes and brains from maxillomandibular impact.							

^a Available to contractors upon originator's approval

DD FORM 1498
1 MAR 68

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 65 AND 1498-1 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE

PROJECT: 3M161102BS10

WORK UNIT TITLE: THE SECONDARY EFFECT OF HIGH VELOCITY MISSILES ON
CRANIOFACIAL TISSUES

PRINCIPAL
INVESTIGATOR: LTC DAVID M. LEWIS, DC

An Evaluation of Eyes and Brain from Laboratory Animals

Wounded in the Maxillofacial Complex with Variable Moss

High Velocity Projectiles

PROBLEM: To conduct a systematic evaluation of animal tissues (eyes and brains) subjected to trauma as a result of high velocity missiles striking the maxillofacial complex. The increasing numbers and velocity of missiles produced by modern weaponry results in a significant increase in the production of tooth and bone fragments which can do extensive damage as secondary missiles remote from the primary missile impact site. The objective of this study is to provide a semiquantitative evaluation of the secondary effects of high velocity missile impacts and to provide data for the "Computer Man" system which will help to define treatment strategies for a wide range of combat wounds.

APPROACH: Forty five Texas Angora goats were shot in the maxillofacial complex with high velocity missiles of various sizes in a USAIDR contract project. At autopsy the eyes and brains were removed intact. Detailed histologic evaluations of these tissues will be made using conventional qualitative methods as well as new methods which will provide which will provide quantitative data.

RESULTS: All goats that did not succumb to missile impact or anesthetic were sacrificed 15 minutes after impact. At autopsy the eyes and brains were removed intact and gross damage was noted. Focal gross brain hemorrhage was noted in four goats. Bony fractures of the base of the skull were found but no bone fragments or tooth fragments were found on gross or xeroradiographic examination of the goat brains. Xeroradiographic techniques were found to be superior to routine radiographs of the brains.

The eyes were prepared for histologic examination. Multiple sections were made from each eye and H&E, PAS and Trichrome stain were done. Ten of the goats had fractures of the orbital bones. Gross hemorrhage of the orbital fat was noted in goat #22828. Microscopic evidence of intra-ocular hemorrhage was found in one goat #22851. That goat had focal mild to moderate hemorrhage of the vitreous body. The source of the blood was most likely the retinal vessels and could have been related to ocular trauma. Other finding indicative of trauma but probably not related to the present test were focal melanosis of the peripheral endothelial cell and filtration angle, cataracts, keratitis, and osseous metaplasia of the posterior sclera. With the exception of the vitreous body hemorrhage in one goat, all of the changes indicative of damage are chronic changes. Since the

goats were sacrificed 15 minutes after impact it must be assumed that the changes noted were not a direct result of the present test. All goats had artifactual retinal separation. No gross or microscopic evidence of bone fragment or tooth fragments were found in any of the eyes examined.

The elongated maxillofacial anatomy minimizes the effect of secondary missile generation (bone & tooth fragments) on the eyes and brains. Because of this anatomic variation the correlation of damage between the goat and human maxillofacial complex is poor.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1 AGENCY ACCESSION ⁶	2 DATE OF SUMMARY ⁶	REPORT CONTROL SYMBOL DD-DR&E(AH)616	
3 DATE PREV SUMMARY ⁴	4 KIND OF SUMMARY	5 SUMMARY SCTY ⁴	6 WORK SECURITY ⁴	7 REGRADING ⁶	8A DWSN INSTR ⁶	8B SPECIFIC DATA: CONTRACTOR ACCESS	9 LEVEL OF SUM A. WORK UNIT
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
10 NO./CODES: ⁶		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
a. PRIMARY		62775A		3S162775A825		AB 014	
b. CONTRIBUTING		62775A		3S162775A825		AC 014	
c. OTHER		STOG: 80-7.2:5					
11 TITLE (Precede with Security Classification Code) ⁶							
(U) Preventive Dentistry Measures of Military Significance							
12 SCIENTIFIC AND TECHNOLOGICAL AREAS ⁶							
012900 Physiology; 002400 Bioengineering							
13 START DATE		14 ESTIMATED COMPLETION DATE		15 FUNDING AGENCY		16 PERFORMANCE METHOD	
71 01		CONT		DA		C. IN-HOUSE	
17 CONTRACT/GRANT				18 RESOURCES ESTIMATE		19 PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE				PRECEDING		b. FUNDS (in thousands)	
b. NUMBER ⁶				FISCAL		82 0.2 21	
c. TYPE				YEAR		CURRENT	
d. KIND OF AWARD				83 0.2 50			
10 RESPONSIBLE DOD ORGANIZATION				20 PERFORMING ORGANIZATION			
NAME: U.S. Army Institute of Dental Research				NAME: U.S. Army Institute of Dental Research			
ADDRESS: Washington, DC 20307				ADDRESS: Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: SWEENEY, T.P.				NAME: LORTON, L.			
TELEPHONE (202) 576-3484				TELEPHONE (415) 561-4845			
21 GENERAL USE				SOCIAL SECURITY ACCOUNT NUMBER POC:DA			
FIC				ASSOCIATE INVESTIGATORS			
				NAME: MADER, C.			
				NAME:			
22 KEYWORDS (Precede EACH with Security Classification Code)							
(U) Marginal Leakage; (U) Resin Restorative; (U) Post and Core Restorations; (U) Dental Emergencies							
23 TECHNICAL OBJECTIVE ⁶ 24 APPROACH. 25 PROGRESS (Furnish individual paragraphs identified by number. Precede last of each with Security Classification Code.)							
23. (U) To develop new and simplified methods of preventing disease related dental emergencies in the field. To assess new methods of (1) improving the biologic management of militarily relevant oral conditions and (2) improving the cost-effectiveness factors of preventive dental therapy in the military.							
24. (U) Studies will be conducted which will (1) develop and evaluate improved methods of dental care which will prevent dental emergencies in the field; (2) develop more rapid and effective means of identifying and treating soldiers with at-risk-profiles for field dental emergencies.							
25. (U) (81 10 - 82 10) A cavosurface margin design in the placement of resin restorations was developed which should decrease marginal leakage, one of the primary causes of restoration failure and resulting dental emergencies. A combined etching procedure and placement of a low viscosity resin demonstrated good adaptation to dentin. This is a first step in developing a clinically satisfactory technique for resin post and core restorations. Improvement of such restorations could reduce field dental emergencies.							

PROJECT: 3S162775A825

WORK UNIT TITLE: PREVENTIVE DENTISTRY MEASURES OF MILITARY SIGNIFICANCE

PRINCIPAL

INVESTIGATOR: LTC LEWIS L. LORTON, DC

Evaluation of a New Restorative Procedure for Resin

Restorations Designed to Prevent Dental Emergencies on the Battlefield

PROBLEM: Marginal leakage is the major cause of failure of resin restorations and may result in a dental emergency. Thousands of resin restorations are placed each year by Army dentists. The development of a technique for resin restorations, which would prevent marginal leakage, is highly desirable as it would prevent the major cause of failure of this commonly used restoration. In addition, it would save time expended by the dental staff and soldier/patient to replace resin restorations that have prematurely failed. It would also prevent dental emergencies associated with restoration failures.

APPROACH: Cavity preparations with traditional and experimental cavosurface margin designs were prepared in extracted human teeth. The margins were etched with orthophosphoric acid (37%) for one minute and then filled with several commercial dental resins. The teeth were dissolved with nitric acid and the cavosurface margins of the remaining, undissolved resin restorations were examined with a scanning electron microscope to evaluate the adaptation of the various resins to the traditional and experimental cavity designs.

RESULTS: One low viscosity resin demonstrated superior adaptation to all experimental cavosurface margin designs. This fine adaptation may prevent marginal leakage around resin restorations done with traditional techniques.

PROJECT: 3S162775A825

WORK UNIT TITLE: PREVENTIVE DENTISTRY MEASURES OF MILITARY SIGNIFICANCE

PRINCIPAL
INVESTIGATOR: LTC CARSON L. MADER, DC

Evaluation of a New Restorative Procedure for Post
and Core Restorations Designed to be More Economical and to
Prevent Dental Emergencies on the Battlefield

PROBLEM: Traditional methods for fabricating post and core restorations are very time consuming and expensive as these techniques require substantial amounts of time from the dentist, the dental assistant, the laboratory technician and the soldier/patient. In addition, relatively large amounts of precious metals (usually gold or a gold alloy) are required. Also, forceful traumatic blows to anterior teeth with cast metal post and core restorations frequently result in fracture of the root. This can easily cause a painful dental emergency requiring immediate removal of the fractured tooth and result in a soldier being lost from duty. The missing anterior tooth must also be eventually replaced. This requires another, multi-step procedure involving additional expense and time expenditure by the dental staff and soldier/patient. The development of a single-step technique for the fabrication of resin post and core restorations could save the Army considerable expense and time expended by the treating dental staff and the soldier/patient. In addition, resin post and core restorations could prevent dental emergencies caused by traumatically induced root fractures associated with traditional cast metal post and core restorations.

APPROACH: Single-rooted, extracted human teeth were treated with conventional endodontic techniques to receive traditional post and core restorations. The canals were then etched with acid and filled with a low viscosity resin. The teeth were longitudinally split in half and examined with a scanning microscope to evaluate the degree of resin penetration into the patent dentin tubules. Reliable and consistent resin penetration of the patent dentin tubules may be the first step in development of a new, one-step, resin technique for fabricating post and core restorations which will be faster, cheaper, and prevent dental emergencies.

RESULTS: Scanning electron microscopic examinations of the canal walls and the resin cores which had formed the canal wall-resin core interface before the teeth were split, showed that the low viscosity resin did effectively penetrate the patent dentin tubules.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)6J6	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8A. ORIGIN INSTR ^a	8B. SPECIFIC DATA - CONTRACTOR ACCESS	9. LEVEL OF SUMMARY
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
10. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER			
a. PRIMARY	62775A	3S162775A825	AB	002			
b. CONTRIBUTING	62775A	3S162775A825	AC	002			
c. 62775A	////////	STOG 80-7.2:5					
11. TITLE (Precede with Security Classification Code) ^a							
(U) Development and Evaluation of Dental Materials and Materiel for Army Use							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
010300 Miscellaneous Materials							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
69 01		CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE: EXPIRATION:				PRECEDING			
b. NUMBER:				FISCAL YEAR		b. FUNDS (in thousands)	
c. TYPE:				82		1.0	
d. KING OF AWARD:				CURRENT		75	
e. CUM. AMT.				83		1.5	
20. RESPONSIBLE DOD ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME: USA Institute of Dental Research				NAME: USA Institute of Dental Research			
ADDRESS: Washington, DC 20012				ADDRESS: Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P., COL, DC				NAME: Vermilyea, S.G., LTC, DC			
TELEPHONE: 202-576-3484				TELEPHONE: 415-752-8343			
				SOCIAL SECURITY ACCOUNT NUMBER POC:DA			
22. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Woolsey, G., LTC, DC			
				NAME: Kuffler, M., B.S.			
23. KEYWORDS (Precede EACH with Security Classification Code) (U) Storage Stability; (U) Composite Restoratives; (U) Impression Materials; (U) Reinforced Resin; (U) Corrosion of Alloys; (U) Porcelain-Metal Bond							
23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)							
23. (U) To evaluate new materials and materiel of special interest to the Army dentist. Criteria for selection of materials, devices or techniques for evaluation are based on anticipated high potentials for: (1) savings of fiscal and/or manpower resources; (2) work simplification; (3) improved health care delivery in combat areas; and (4) enhanced safety with respect to professional and ancillary personnel as well as to the patient.							
24. (U) New materials will be evaluated on the basis of the following parameters: Composition, microstructure, physical and mechanical properties, cytotoxicity, and clinical performance.							
25. (U) (81 10 - 82 10) The storage stability of 5 composite restoratives and 9 impression materials were subjected to cyclic temperature-humidity conditions for 5 months. One composite lost tensile strength and one lost setting characteristics. All the impression materials showed some changes. Continued work with carbon fiber reinforced acrylic resin indicates potential use for the stabilization of maxillofacial fractures or field repair of prostheses. A method of identifying potential corrosion problems in biomedical alloys used by the Army is being developed and is near completion. The development of a procedure to improve porcelain-to-metal bonds is in progress. Some success has been obtained to date. Potential savings in fiscal and manpower expenditures that could result from this latter effort are considerable.							

PROJECT: 35162775A825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND
MATERIEL FOR ARMY USE.

PRINCIPAL
INVESTIGATOR: LTC S. G. VERMILYEA, DC

Storage Stability of Dental Materials of Interest to the
Military Dentist

PROBLEM: Logistical burdens inherent to the world wide deployment of military dentists are manifold. Among the most prominent problems are those related to the shipment and storage of certain restorative materials. For example, organoinorganic composites, waxes and elastomeric impression materials which can be employed successfully throughout the North American continent may not survive shipment to less temperate regions. In addition, the extent to which prolonged storage under tropical, arid or arctic-like conditions might affect the properties and characteristics of these materials is unknown. At the present time there is no rapid "aging" test to assess the potential storage characteristics of materials.

APPROACH: A programmable temperature/humidity chamber was used to simulate extremes of tropical, subtropical and arctic-like climatic conditions. Unopened, "as received" packages of selected materials will be exposed to each storage condition of periods ranging from two to six months. At the termination of each storage period the materials were subjected to standard tests to assess their physical and mechanical properties and manipulative characteristics. The features of the stored materials were compared to those of the "as received" materials.

RESULTS: In this initial portion of the study, five composite restoratives and nine impression materials were subjected to cyclic temperature/humidity conditions. When compared to the base line values the compressive strength values for the composite restoratives were not significantly altered by exposure to a temperature/humidity cycle (-10° to 46°C and 50-89% respectively) for five months. Tensile (diametral compressive) strength of one material (Adaptic) decreased more than 50% subsequent to the same cycle. In addition, one material (Profile) exhibited a slight deterioration of its setting characteristics after five months. With the impression materials, exposure to the temperature/humidity cycle elicited a general increase in permanent deformation for the polysulfides and one of the vinylpoly-siloxanes. Increased 24 hour dimensional change was observed with all of the materials except one vinylpolysiloxane and the polyether product. The properties of the polyether material were not altered by the temperature-humidity cycle. It should be noted that the observed changes in the materials are measurable in the laboratory but may not be of great clinical significance. Additional work is needed to alter the temperature/humidity program to (a) more closely duplicate expected field conditions (b) shorten the time required to produce property changes and (c) correlate the accelerated aging program with the expected shelf life as defined by the product manufacturer.

PROJECT: 3S162775A25

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND
MATERIEL FOR ARMY USE

PRINCIPAL
INVESTIGATOR: LTC S. G. VERMILYEA, DC

Effects of Fiber Reinforcement on the Dynamic

Properties of Denture Base Resins

PROBLEM: Flexural fatigue fracture of acrylic denture bases are not uncommon occurrences. Solution to this problem often requires the construction of cast metal bases; a difficult, relatively expensive and time consuming task. Increases in the flexural fatigue resistance of acrylic denture bases would reduce the need for metal based dentures, allow thinner prostheses to be used in conjunction with soft lining materials and permit the use of thinner yet rigid stents during intraoral stabilization of fractures.

APPROACH: Silanized and unsilanized carbon fibers were processed longitudinally, perpendicularly, in a criss-cross pattern, as well as randomly to the long axis of acrylic specimens. The specimens were machined to a size of 60mm X 10mm X 2.5mm and subjected to three point cyclic loading at a rate of 325 cycles per second under a 5kg load until failure occurred. Additional specimens were subjected to transverse and tensile strength determinations.

RESULTS: The data indicate that a 100% increase in fatigue strength and transverse strength is possible with silanized longitudinal fibers placed in the center of the specimen. However, this is a technically difficult task. The use of 0.4% by weight of randomly dispersed chopped (3-4mm length) fibers resulted in an 80% increase in fatigue strength without adversely affecting the other properties. It is conceivable that the incorporation of chopped fibers into prepackaged denture repair materials would also provide similar property increases at minimal cost. At this time this project is complete.

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND
MATERIEL FOR ARMY USE

PRINCIPAL
INVESTIGATOR: LTC S. G. VERMILYEA, DC

Electrochemical Profiles of Dental Alloys

PROBLEM: World wide deployment of biomedical materials and materiel subject these items to extreme conditions and increase their potential for tarnish and corrosion. Currently, there is no rapid, reliable method for the prediction of the potential corrosion resistance of equipment and supplies in a given environment nor the potential useful life of many metallic supplies. Furthermore, many biomedical alloys, when placed in contact with living tissue undergo dissolution with the subsequent release of ion species potentially toxic to the host tissues. A method of identification of the potential corrosion resistance of biomedical materials and materiel would be invaluable to the rational selection of the most stable and safest items for use by the U.S. Army Health Care Delivery System.

APPROACH: Initially, a study will be undertaken to determine appropriate specimen geometry and finishing technique to yield reproducible results. Subsequently, potentiodynamic polarization, linear polarization (corrosion rate determination) and galvanic coupling procedures will be combined with formed film analysis to determine the species of ions released and the potential corrosion resistance of the test materials.

RESULTS: A specimen geometry and metal finishing procedure has been developed which appears to produce consistent results. Briefly, cast disc specimens are mounted in a thermoplastic medium and polished metallographically with 0.3 micrometer alumina. Subsequent to each electrochemical determination, the specimens were repolished with 0.3 micrometer alumina. The use of the technique with several base metal alloys has given reproducible results. The remainder of electrochemical techniques will be initiated upon receipt of the necessary instrumentation on the West Coast.

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND
MATERIEL FOR ARMY USE

PRINCIPAL
INVESTIGATOR: LTC S. G. VERMILYEA, DC

Effects of Alloy Surface Treatment on the
Porcelain-Metal Bond

PROBLEM: Ceramo-metal restorations account for a significant portion of the fiscal expenditures within the Army Health Care Delivery System. The rapidly fluctuating price of gold and other noble metals has prompted intense interest in the use of less costly base-metal alloys as alternative to the high noble content materials. Savings of 80-90% in current alloy expenditures are possible with the use of base-metal materials. Unfortunately, a significant draw back to the use of these materials has been the frequent failure of the porcelain-alloy bond. Such failure requires refabrication of restorations with concomitant additional expenditure of fiscal and manpower resources. The mode of failure (i.e., cohesive within the metal oxide layer or adhesive at the oxide-metal phase boundary) suggest the possibility of modifying the substrate metal surface prior to porcelain application to improve the integrity and strength of the porcelain-alloy bond.

APPROACH: Selected base metal alloys and proprietary coating agents were used in a randomized design to determine the effects of the coating agent on the strength of the porcelain-metal bond. Specimens were 1/4 X 1/16 inch cast discs to which porcelain was applied in the shape of a cylinder. The porcelain cylinder was embedded in a tray acrylic and the disc subjected to diametral loading at a cross head descent rate of 0.02 inch per minute. The apparent porcelain alloy bond strength was calculated on the basis of the apparent area of porcelain alloy contact and the load at shear failure.

RESULTS: With two of the alloys, the use of a metal conditioning or coating agent prior to porcelain application had no effect on the apparent bond strength over that observed with uncoated specimens. With one alloy, the use of the bonding agent resulted in a decrease in apparent bond strength as compared to specimens in which the coating agent was not used, whereas the remaining alloy exhibited the similar bond strength values with any of the coating agents. Examination of the failure sites indicate a metal-oxide or oxide-oxide type of failure. Further work is in progress to develop new finishing procedures, firing cycles and a proprietary "bonding agent" to overcome the difficulty in obtaining a reliable porcelain-alloy bond with the base metals. In addition, the effects of different porcelains with the various alloys will be assessed.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ¹	2. DATE OF SUMMARY ²	REPORT CONTROL SYMBOL DD-DR&E(AR)436	
3. DATE PREV SUMMARY 81 10 01	4. KIND OF SUMMARY D. CHANGE	5. SUMMARY SCTY ³ U	6. WORK SECURITY ⁴ U	7. REGRADING ⁵	8A. DES'N INSTR'N NL	8B. SPECIFIC DATA- CONTRACTOR ACCESS <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	9. LEVEL OF SUM A. WORK UNIT
10. NO./CODES ⁶		PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER		WORK UNIT NUMBER	
a. PRIMARY		62775A	3S162775A825	AB		003	
b. CONTRIBUTING		62775A	3S162775A825	AC		003	
c. CONTRIBUTING		//////////	STOG 80-7.2:5				
11. TITLE (Proceed with Security Classification Code) ⁷ (U) Development and Improvement of Metallic Restorative Materials							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ⁸ 009900 Metallurgy and Metallography							
13. START DATE 69 01		14. ESTIMATED COMPLETION DATE CONT		15. FUNDING AGENCY DA		16. PERFORMANCE METHOD C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE:		EXPIRATION:		PRECEDING		b. FUNDS (in thousands)	
a. NUMBER: ⁹				FISCAL		82 1.0 54	
c. TYPE:		d. AMOUNT:		YEAR		CURRENCY	
e. KIND OF AWARD:		f. CUM. AMT.		83		1.0 65	
20. RESPONSIBLE ODO ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME: ¹⁰ USA Institute of Dental Research				NAME: ¹¹ USA Institute of Dental Research			
ADDRESS: ¹² Washington, DC 20012				ADDRESS: ¹³ Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P.				NAME: ¹⁴ Vermilyea, S.			
TELEPHONE: 202-576-3484				TELEPHONE: 415-752-8343			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
22. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Woolsey, G.			
				NAME: Kuffler, M.			
23. KEYWORDS (Proceed EACH with Security Classification Code) (U) Base Metal Alloys; (U) Casting Accuracy; (U) Soldering Base Metals; (U) Investment Techniques.							
24. TECHNICAL OBJECTIVE, ¹⁵ 25. APPROACH, 26. PROGRESS (Furnish individual paragraphs identified by number. Proceed rest of each with Security Classification Code.)							
23. (U) Annual Army expenditures for precious metals utilized in the fabrication of fixed dental prostheses are in the vicinity of \$1,000,000. The cost of an equal volume of base metal alloy is \$30,000. Properties of base metal alloys indicate however that these alloys cannot be utilized for small castings without drastic metallurgical modifications. This work is therefore being conducted to (1) develop heat treatment methods for controlling properties of nickel-chromium based casting alloys; (b) evaluate nickel-chromium based alloys for use in operative dentistry.							
24. (U) The properties of nickel-chromium based alloys will be studied in detail by various physical methods available in order to devise procedures which will optimize their usefulness. Any improvement obtained will be evaluated clinically.							
25. (U) (81 10 - 82 10) Reliable methods for casting base-metal alloys as replacements for noble metals have been lacking. A study completed on 6 commercially available base metal alloys showed that the casting accuracy of 5 alloys could be dramatically improved by modifying investment techniques. The techniques developed are reliable and simply applied. The resulting savings in money and manpower should be significant. Attempts to develop reliable techniques for soldering base-metal alloys have thus far not been successful. Studies are continuing.							

PROJECT: 3S162775A825

UNIT WORK TITLE: DEVELOPMENT AND IMPROVEMENT OF METALLIC RESTORATIVE MATERIALS

PRINCIPAL
INVESTIGATOR: LTC S. G. VERMILYEA, DC

Development of Techniques to Improve the
Casting Accuracy of Base-Metal Alloys

PROBLEM: Although the potential fiscal savings to be realized through the use of base metal alloys in military dental practice is great, several problems need to be addressed prior to the institution of their routine. Among the problem areas is the development of methods for the routine accurate casting of these alloys by personnel of varying skill levels.

APPROACH: Commercially available investment materials were employed in modified investing techniques to construct full coverage restorations. Investment materials included Hi-Temp 2 and Ceramigold 2. Modifications to investing techniques were hydroscopic methods, alteration of special liquid concentrations (Hi-Temp) and the use of Hi-Temp and Ceramigold special liquid at selected dilutions with Hi-Temp 2 and Ceramigold 2 investments. Two hundred twenty two wax patterns were constructed on individual stone dies, invested and cast in Unibond, Ceramalloy II, Biocast and Neobond II alloy. After divestment each casting was seated on its die and examined for size and marginal integrity with the aid of examining loupes. Castings were judged as: adequate (0); oversize (+); or under size (-).

RESULTS: When casting size was the determining factor the scores for the total sample distribution were: (+) - 49%; (0) - 32% (-) - 29%. When marginal integrity was considered the scores were: (+) - 21%; (0) - 22%; (-) - 57%. Investment manufacturer's with 62% special liquid in a hydroscopic technique produced consistently well-fitting castings with Unibond, Ceramalloy II and Biocast. In addition, 100% and 83% of the respective castings of Unibond and Biocast from Ceramigold 2 molds using 23% special liquid and a non-hydroscopic technique were adequate. None of the technique modifications produced consistently well-fitting castings from Neobond II alloy. The findings suggest that investing techniques must be tailored to the characteristics of the individual alloy.

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND IMPROVEMENT OF METALLIC RESTORATIVE MATERIALS

PRINCIPAL

INVESTIGATOR: LTC S. G. VERMILYEA, DC

Tissue Response to Base-Metal Crown and Bridge Alloys

PROBLEM: The military is under constant pressure to reduce fiscal expenditures for noble alloys. In addition, laboratories and purchasing agents are inundated by alloy manufacturers to purchase a particular product and must do so if a "low bid" is received from a particular manufacturer. Alloys of seemingly similar composition differ markedly in their potential histotoxic reactions. It would appear that the severity of any tissue reaction depends upon the cytotoxic potentials of ions made available through dissolution of products produced by wear and corrosion of the alloy's surface. Since, in the military, the dental population is "captive" and has little choice as to the type of alloy employed, it is important that alloys of known safety and efficacy be used in the Military Health Care Delivery System.

APPROACH: Powders obtained from the wet-milling of five alloys will be pressed into tablets, sterilized and implanted subcutaneously in rats. Specimens will be harvested at 1 week, 1 month, 2 months, 6 months, and one year. The tissues will be processed and graded as to the severity of inflammatory response.

RESULTS: To date, powders of two of the alloys have been produced. Additional preparation will commence upon receipt of appropriate equipment.

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND IMPROVEMENT OF METALLIC RESTORATIVE MATERIALS

PRINCIPAL

INVESTIGATOR: LTC S. G. VERMILYEA, DC

Development of Techniques for the Soldering of Base-Metal Alloys

PROBLEM: The potential fiscal savings to the U.S. Army Health Care Delivery System afforded by the use of base-metal alloys in lieu of expensive noble materials has been well established. Heretofore, technology for the routine accurate casting of many of these alloys has been developed within this laboratory. However, many times an intraoral dental prosthesis must be joined by soldering prior to completion. Controversy exists as to the most appropriate soldering method and the degree of success to be expected. Development of a predictably successful soldering technique for use with base-metal alloys will permit full realization of the potential fiscal savings afforded by the use of base-metal alloys in Army Area Dental Laboratories.

APPROACH: Initially five base-metal alloys and five solders were employed in a randomized design to assess the effects of each solder/alloy combination on the tensile strengths of the resultant joints. Specimens were half-tensile bars fabricated from the substrate alloys by conventional dental laboratory procedures. Soldering of each alloy/solder combination was accomplished in accordance with the solder manufacturer's instructions. Soldered bars were subjected to tensile loading on a testing machine at a crosshead speed of 0.02 inch per minute. Strength and rigidity of the specimens were assessed by analysis of the resultant load deflection curves.

RESULTS: The results indicate that the successful soldering of base-metal alloys is variable at best. Fully 38% of the specimens fractured prior to testing. Of the successfully tested specimens, tensile strength values ranged from 4,500psi alloy with Unibond Pre-Solder. Precision of the data was low with coefficients of variation ranging from 1 to 54%. In general, the ability to produce consistently strong contiguous solder joints from any alloy/solder combination was poor. Surface and subsurface porosity was a characteristic feature of the solder joints. Studies are now in progress to develop pre-soldering finishing procedures and alternative fluxing agents to improve the wetting characteristics of the solder on the substrate alloy and hopefully the strength and integrity of the solder joint.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a		2. DATE OF SUMMARY ^a		REPORT CONTROL SYMBOL DD-DR&E(AR)636	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8. DES'N INSTR ^a	9. SPECIFIC DATA - CONTRACTOR ACCESS		10. LEVEL OF SUM	11. WORK UNIT
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO			
12. NO./CODES ^a		PROGRAM ELEMENT		PROJECT NUMBER		TASK ARE NUMBER		WORK UNIT NUMBER	
a. PRIMARY		62775A		3S162775A825		AA		010	
b. CONTRIBUTING		62775A		3S162775A825		AB		010	
c. DATE/NO./YR		////////		STOG 80-7.2:5					
13. TITLE (Precede with Security Classification Code) ^a									
(U) The Initial Treatment of Combat Wounds									
14. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a									
012600 Pharmacology 012900 Physiology 002300 Biochemistry									
15. START DATE			16. ESTIMATED COMPLETION DATE			17. FUNDING AGENCY		18. PERFORMANCE METHOD	
81 01			CONT			DA		C. IN-HOUSE	
19. CONTRACT/GRANT				20. RESOURCES ESTIMATE		21. PROFESSIONAL MAN YRS		22. FUNDS (In thousands)	
a. DATES/EFFECTIVE:				b. NUMBER ^a		c. TYPE:		d. AMOUNT:	
a. KIND OF AWARD:				f. CUM. AMT.		fiscal year		currency	
						82		1.0	
						83		1.0	
								77	
								90	
23. RESPONSIBLE DOD ORGANIZATION					24. PERFORMING ORGANIZATION				
NAME ^a USA Institute of Dental Research					NAME ^a USA Institute of Dental Research				
ADDRESS ^a Washington, DC 20012					ADDRESS ^a Washington, DC 20012				
RESPONSIBLE INDIVIDUAL					PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)				
NAME: Sweeney, T.P.					NAME ^a Wynkoop, J.				
TELEPHONE: 202-576-3484					TELEPHONE: 202-576-3393				
					SOCIAL SECURITY ACCOUNT NUMBER: POC:DA				
25. GENERAL USE					ASSOCIATE INVESTIGATORS				
Foreign Intelligence Considered					NAME: Setterstrom, J.				
					NAME: Vincent, J. Miller, R.				
26. KEYWORDS (Precede EACH with Security Classification Code) (U) Cellulose Triacetate; (U) Gentamicin; (U) Copolymer Bandage; (U) Lidocaine; (U) Laboratory Animals									
27. TECHNICAL OBJECTIVE, 28. APPROACH, 29. PROGRAM (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)									
23. (U) To develop a multipurpose wound dressing which will provide anesthesia, antiseptics and hemostasis so that, where appropriate, the result will be rapid return of the wounded soldier to duty as well as reduction of the morbidity occasioned by delayed definitive treatment and secondary complications.									
24. (U) Contract developed drug release systems will be evaluated in animal models developed specifically for that purpose. Various methods and materials for maintaining contact over a variety of maxillofacial contours will be evaluated for their utility of application and use in the combat situation.									
25. (U) (81 10 - 82 10) A biodegradable polylactic-polyglycolic acid copolymer fabric matrix containing the anesthetic lidocaine was evaluated in a rabbit model for its ability to provide an extended analgesic effect. Based on tactile responses in the experimental animals it was demonstrated that a wound covering can be produced which will deliver appropriate drug levels over a 24 hour period. A new cellulose triacetate material is being evaluated as an antibiotic delivery system for incorporation into bandages. In vitro tests indicate the material is a good slow-release medium for bactericidal agents. A wound model has been established in guinea pigs and a cellulose triacetate-gentamicin system is being evaluated on these wounds for its ability to treat S. aureus infections.									

PROJECT: 3S162775A825

WORK UNIT TITLE: THE INITIAL TREATMENT OF COMBAT WOUNDS

PRINCIPAL
INVESTIGATOR: CPT JUDSON R. WYNKOOP, DC

Development of a Multipurpose Wound

Dressing for the Soldier

PROBLEM: Despite advances made during the past thirty years in our understanding of the healing process, the lack of an adequate wound dressing or bandage persists. There is a need for a multipurpose wound dressing, adaptable to combat situation, which will provide anesthesia, antiseptis, and hemostasis.

APPROACH: A biodegradable fabric will be used as a matrix for extended release anesthetic and antiseptic products. Anesthetic and antiseptic materials will be evaluated prior to combination with the matrix. Serum levels of anesthetic will be measured at 0, 10, 30 minutes and at 1, 2, 4, 6, 10 and 24 hours following injection of extended release materials and compared to serum levels following injection of standard as well as commercial local anesthetic solutions. The tactile responses of animals will be measured following injection of standard and commercial solutions and compared with the tactile responses following injection of extended release anesthetics. A separate model system, using rats, will be developed to measure the antiseptic quality of extended release products.

RESULTS: Preliminary data indicate that an extended release local anesthetic can be manufactured which will deliver measurable quantities over a 24-hour period. Further evaluation of products manufactured under contract is in progress and should demonstrate the maximum serum levels obtainable with slow release local anesthetics.

PROJECT: 3S162775A825

WORK UNIT TITLE: THE INITIAL TREATMENT OF COMBAT WOUNDS

PRINCIPAL
INVESTIGATOR: JEAN A. SETTERSTROM, PhD

Investigation of a New Cellulose

Triacetate Film As A Wound Dressing

PROBLEM: Wound dressing technology has not advanced in recent years at a pace consistent with the technology available for its improvement. Minor wounds in mass casualty situations tend to receive little attention. However, wounds which do not initially prevent the soldiers from performing his duties are often the occasion for infections which ultimately result in significant lost duty time. Wound dressings are required which not only provide hemostasis but also relatively long term prevention or elimination of infections. This would reduce treatment time, morbidity and performance decrement.

APPROACH: Extended drug release technology offers a solution to the prevention or elimination of infections in minor wounds through the incorporation and zero-order release of medicaments from appropriately designed wound dressing materials. A new cellulose triacetate film with an extremely high porosity is being studied for its ability to release antibiotics over an extended period into standardized wounds in guinea pigs infected with known levels of Staphylococcus aureus. This wound model will be used to determine the release kinetics and anti-infection capabilities of films loaded at various levels with different antibiotics.

RESULTS: A wound model has been devised that consists of surgically created one inch square, full thickness wounds on the backs of guinea pigs. Each wound is contaminated with a broth suspension containing 2.5×10^{10} S. aureus. Wounds are covered with the cellulose triacetate film and at 3 days post-wounding the film is removed and the wound is scrubbed with a buffer-detergent mixture and the wash is assayed for bacterial content. Tissue is also removed from each wound site and assayed for bacterial content. Under those conditions using unloaded cellulose triacetate films a mean bacterial level of 6.5×10^7 is assayed in the wash solutions and in excess of 10^5 organisms/gm in the tissues assayed. Cellulose triacetate films are currently being prepared under contract. Films with various loadings of gentamicin and possibly clindamycin will be evaluated in the above animal model.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL	
				DA OG 8670	82 10 01	DD-DR&E(AR)8J6	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY ICTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8. DISB'N INSTR'M	9a. SPECIFIC DATA- CONTRACTOR ACCESS	9. LEVEL OF SUM
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
10. NO./CODES ^a		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
a. PRIMARY		62775A		3S162775A825		AB 011	
b. CONTRIBUTING		62775A		3S162775A825		AC 011	
c. Contributing		STOG 80-7.2:5					
11. TITLE (Precede with Security Classification Code) ^a (U) Development and Evaluation of Dental Materiel for Field Use.							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
002400 Bioengineering 010300 Miscellaneous Materials							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
81 10		CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE:				PRECEDING		b. FUNDS (in thousands)	
b. NUMBER: ^a				FISCAL YEAR		82 0.5 165	
c. TYPE:				CURRENCY		83 2.0 165	
d. KIND OF AWARD:				f. CUM. AMT.			
19. RESPONSIBLE DOD ORGANIZATION				20. PERFORMING ORGANIZATION			
NAME: ^a USA Institute of Dental Research				NAME: ^a USA Institute of Dental Research			
ADDRESS: ^a Washington, DC 20012				ADDRESS: ^a Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P.				NAME: ^a Lorton, L., LTC, DC			
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				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
21. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Vandre, R. RETHMAN, M.			
				NAME: Grover, P.			
22. KEYWORDS (Precede EACH with Security Classification Code) ^a (U) Dental X-ray; (U) Dental Cutting Instrument; (U) Subtraction Radiography; (U) Radionuclide X-ray System; (U) Laboratory Animals							
23. TECHNICAL OBJECTIVE, ^a 24. APPROACH, 25. PROGRAM (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)							
23. (U) To assist in the development of dental equipment capable of reliable performance and easy maintenance under all field operational conditions. Included are the development of concepts for field dental equipment which is miniaturized, lightweight, energy efficient and low cost.							
24. (U) Conceptual and basic engineering requirements for a field dental x-ray system and a field dental cutting instrument will be studied. Current technology will be reviewed for its ability to produce the needed design criteria and advanced technology requirements will be identified. Experimental devices will be constructed.							
25. (U) (81 10 - 82 10) Studies have been initiated on the development for field use of (1) a hand-held, battery-operated, real-time dental x-ray system; (2) a radionuclide based dental x-ray system, and (3) a field dental cutting instrument based on fluidic principles. A "bread board" lightweight, battery-operated, real-time x-ray has been evaluated clinically and found to produce excellent real-time imaging. Prototype designs have been submitted for construction under contract. The application of computerized subtraction radiography as a means of improving the detection of hard tissue wounds is being evaluated <i>in vivo</i> . Osseous wounds have been created in dog mandibles and the data are being evaluated.							

^a Available to contractors upon originator's approval

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIEL FOR FIELD USE

PRINCIPAL
INVESTIGATOR: LTC LEWIS L. LORTON, DC

A Dental X-Ray System for Field Use

PROBLEM: The current field dental x-ray apparatus is heavy, bulky, and has a high energy consumption. The dependence on conventional film and developing is also inefficient in a field situation. New concepts are required for producing dental x-rays in the field which are miniaturized, light-weight, energy efficient and cost effective. The energy requirement is a particularly pressing problem inasmuch as an ever-increasing demand for energy must be met for the wide variety of energy-intensive equipment used in the field. Self-contained equipment with independent energy sources must be developed if maximum utility and flexibility are to be maintained. Likewise, weight and cubic displacement are important to withstand the rigors of the field with minimal maintenance and down-time.

APPROACH: Two concepts are being evaluated with respect to energy sources. One is a battery operated system; the second is a radionuclide driven system. Current technology is being evaluated and correlated with user interface to determine if real-time imaging or a dry film (e.g. Polaroid) approach are sufficient for the diagnostic requirements of the field. Current technology is also being evaluated for miniaturization and weight reduction potential.

RESULTS: A real-time x-ray device utilizing an advanced battery system, a gadolinium oxy-sulfide x-ray detector screen and a small x-ray source operating at 40kvp was evaluated in a "bread-board" configuration for its ability to visualize endodontic procedures performed in monkeys. A total area of approximately 1 square inch could be seen with sufficient clarity to accurately determine the results of the root canal procedures. Subjective evaluation by a number of dentists indicated that the level of diagnostic information obtained was good to excellent. The total system weighed just under 20 lbs. A second system currently in the design stage is based on the use of a radionuclide as an energy source. A mock-up x-ray device has been constructed which weighs less than 1 lb and has a cubic volume of less than 27 cubic inches. The energy source proposed for this device is a gadolinium nuclide with a useful half-life of approximately one year. The source will be contained in a tantalum shield with a "dead-man" switching device for producing the x-ray exposures. Exposures will be recorded on extremely fast Polaroid film. All calculations have been completed and the test sources are being ordered.

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIEL FOR FIELD USE

PRINCIPAL
INVESTIGATOR: LTC LEWIS L. LORTON, DC

Development of a Field Dental Cutting System

PROBLEM: Currently available field dental units, although considerably reduced in size and weight compared to fixed installations, are still amenable to further improvements to include reductions in size, weight and overall portability. Current technology should also provide a means of making the equipment more rugged and maintenance free. These improvements are essential in view of the overall burden placed on logistical support on the modern battlefield.

APPROACH: Current engineering technology will be evaluated for application to the requirements of the dental cutting system which provides the driving force for the cutting instrument itself. Principles developed in fluidic technology will be used as the basis for developing a more rugged maintenance free system as well as reducing overall size and weight. The system will be constructed by the Harry Diamond Laboratory.

RESULTS: A series of preliminary design criteria have been prepared which will be directed initially at elimination of much of the flexible tubing in the current system since this is its most damage prone area. Much of the remaining effort has been directed at consolidation and repackaging for strength, reduced weight, and reduced cube. Construction of the preliminary design will begin in FY83.

PROJECT: 3S162775ZA825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF DENTAL MATERIEL FOR FIELD USE

PRINCIPAL
INVESTIGATOR: MAJ MICHAEL P. RETHMAN, DC

Computerized Subtraction Radiography in the Diagnosis of
Bone Wounds in Dogs

PROBLEM: Studies have shown that enormous amounts of bony destruction are undetectable on conventionally viewed sequential radiographs. It has also been shown that the effect of a complex background of unchanged radiopaque material complicates the detection of subtle changes. Significant destruction of hard tissues due to infection can often progress undetected with the result that treatment time as well as lost duty time for the wounded soldier are increased. A radiographic system which can provide early detection of bony destruction due to infection could be of considerable value in a field hospital. A technique has been developed whereby the detection of subtle osseous changes is facilitated in sequential standardized radiographs. Imagery remaining after this processing represents only changed structures in this longitudinal effort. Investigations have shown improved diagnostic capability in dry skulls using this methodology. The efficacy of this technique has not been demonstrated in a live model nor does equipment or methodology exist to this end. The purpose of this investigation is to develop necessary equipment and methodology to execute a study comparing computer subtraction technique with conventional radiographic techniques in live models.

APPROACH: Highly standardized (geometric and densitometric) radiographs are a necessity for this study. Rigid interfacing devices are to be designed and built for use in the dog model. Methods of mathematical error assessment are to be included. Osseous lesions (as wound analogs) are to be induced in dog mandibles. Preoperative and postoperative radiographs are to be compared as described in the PROBLEM statement. Statistical analysis of this comparison data will be generated. Analysis of the ability of designed equipment and method to the end of highly standardized radiographs will also be accomplished.

RESULTS: Preliminary results indicate that the equipment and methodology developed for use in the dog will generate quality radiographs for use in the study. Error assessment devices have been included in the equipment and have demonstrated levels of geometric standardization in accuracy unapproached in the past. Densitometric standardization analyses are presently underway. Two of the eight dogs are in the healing phase (postoperative) of the study. The remaining six dogs are scheduled for wound induction in November 1982.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)636	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8. DISSEM INSTR ^a	9. SPECIFIC DATA - CONTRACTOR ACCESS	10. LEVEL OF SUM A. WORK UNIT
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
10. NO./CODES: ^a		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
a. PRIMARY		62775A		3S162775A825		AB	
b. CONTRIBUTING		62775A		3S162775A825		AD	
c. OTHER/OTHERS ^a		//////////		STOG 80-7.2:5		013	
11. TITLE (Precede with Security Classification Code) ^a							
(U) Epidemiological Investigation of Dental Emergencies							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
012900 Physiology 012600 Pharmacology							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
81 10		CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE			
a. DATES/EFFECTIVE:				PRECEDING			
b. NUMBER: ^a				FISCAL YEAR			
c. TYPE:				82			
d. KIND OF AWARD:				CURRENCY			
e. AMOUNT:				83			
f. CUM. AMT.				1.0			
				1.2			
				40			
				75			
19. RESPONSIBLE DOD ORGANIZATION				20. PERFORMING ORGANIZATION			
NAME: ^a USA Institute of Dental Research				NAME: ^a USA Institute of Dental Research			
ADDRESS: ^a Washington, DC 20012				ADDRESS: ^a Division of Clinical Operations			
				Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Precede with Security Classification Code) ^a			
NAME: Sweeney, T.P.				NAME: ^a Lewis, D.			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3258			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
21. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Carpenter, W.M.			
				NAME: Grover, P.			
22. KEYWORDS (Precede Each with Security Classification Code) (U) Lip Pathology; (U) Herpetic Lesions; (U) Cold Weather Survey; (U) Xerocheiliosis							
23. TECHNICAL OBJECTIVE, ^a 24. APPROACH, 25. PROGRESS (Precede individual paragraphs identified by number. Precede text of each with Security Classification Code.)							
<p>23. (U) To determine the causes of dental emergencies in a population of soldiers receiving regular dental care and to determine "at-risk-profiles" for those soldiers in critical occupation specialties so as to minimize problems with dental casualties during deployment.</p> <p>24. (U) Studies will be conducted among soldier populations to pinpoint the causes of dental emergencies, their frequency and diagnostic strategies which will permit the prediction of the potential of each soldier for such emergencies. The goal is to select out the "at-risk" group for dental treatment and thus minimize dental casualties during deployment.</p> <p>25. (U) (81 10 - 82 10) Cold weather surveys conducted at Ft Drum, New York were completed in January 1982. A total of 1422 soldiers were surveyed. Preliminary analysis of data reveals there were 71% in the 20-29 age range, 98.5% were male and 78% spent 50% or more time outdoors. The incidence of acute xerocheilosis was found to be 1.1%. The incidence of herpetic lip lesions was 3.1%. There is no marked difference in incidence rate when compared to complexion. Incidence rates increase with severity of weather and increased exposure. The use of protective medication did not decrease the incidence of acute lip damage.</p>							

^a Available to contractors upon originator's approval.

PROJECT: 3S162775A825

WORK UNIT TITLE: EPIDEMIOLOGICAL INVESTIGATIONS OF DENTAL EMERGENCIES

PRINCIPAL

INVESTIGATOR: LTC DAVID M. LEWIS, DC

The Prevalence of Environmentally Induced Lip Pathology

Among Active Duty Soldiers: A Cold Weather Survey

PROBLEM: This study is necessary in order to establish base line data relative to the prevalence of lip pathology among the active duty military population. No data exist that identifies the prevalence of lip pathology among active duty service personnel and is related to occupational exposure to environmental factors. Military operations frequently require exposure of soldiers to extreme environment conditions for prolonged periods of time. While the acute problems do not usually constitute a medical emergency they do present problems with voice transmission, nutrition and morale.

APPROACH: This is a survey of active duty personnel on field training exercises during adversely cold weather conditions. The age, sex, duty environment, complexion, and lip condition will be recorded and weather conditions correlated.

RESULTS: It appears that while actinic exposure is an etiologic factor in acute lip injury, the relative humidity of the environment is even more significant. Acute lip damage is prevalent among troops exposed to adverse environments. Appreciable amounts of acute damage were found in cold environments and hot dry climates. The data do not support the hypothesis that sun exposure (actinic radiation) is the major risk factor. Relative humidity appears to be a more significant factor based on both the hot weather and cold weather survey data. The modifying effects of complexion were significant in cold weather, dark complexion is a risk factor, while it is a protective factor in hot weather. Age and amount of time spent outdoors are not significant risk factors in acute cold weather lip injury. Based on these findings, the use of emollient preparations is recommended. Such preparations should protect the lips from acute lip damage caused by dessication in a dry climate regardless of the temperature.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL	
				DA OG 8674	82 10 01	DD-DR&E(AR)6J6	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8. DISEM INSTR ^a	9. SPECIFIC DATA- CONTRACTOR ACCESS	10. LEVEL OF SUM
81 10 01	H. TERM	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
11. NO./CODES ^a		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
a. PRIMARY		62775A		3S162775A825		AA 012	
b. CONTRIBUTING		62775A		3S162775A825		AB 012	
c. CONFIDENTIAL ^a		//////////		STOG 80-7.2:5			
11. TITLE (Precede with Security Classification Code) ^a (U) Development and Evaluation of Methods and Materials for Treating Traumatic Injury							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
010300 Miscellaneous Materials 002400 Bioengineering							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
81 10		82 09		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE:				PRECEDING		b. FUNDS (in thousands)	
b. NUMBER ^a				FISCAL YEAR		c. FUNDS (in thousands)	
c. TYPE:				82		1.0	
d. KIND OF AWARD:				83		00	
e. AMOUNT:				CURRENCY			
f. CUM. AMT.							
20. RESPONSIBLE DOD ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME ^a USA Institute of Dental Research				NAME ^a USA Institute of Dental Research			
Washington, DC 20012				Division of Oral Biology			
ADDRESS ^a				Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P.				NAME ^a Tortorelli, A.			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3764			
22. GENERAL USE				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
Foreign Intelligence Considered				ASSOCIATE INVESTIGATORS			
				NAME: Vermilyea, S.			
				NAME:			
23. KEYWORDS (Precede EACH with Security Classification Code) (U) Polymer Devices; (U) Ceramic Devices; (U) Biodegradable Polymers; (U) Biodegradable Ceramic							
24. TECHNICAL OBJECTIVE ^a 25. APPROACH. 26. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)							
23. (U) To develop the technology and methodology for applying synthetic materials to the effective management of maxillofacial injuries in the field.							
24. (U) Biodegradable and partly biodegradable polymeric and ceramic devices will be designed and constructed. Designs will be directed at providing the potential for simplifying the management of maxillofacial wounds from the point of initial injury through early definitive treatment.							
25. (U) (81 10 - 82 10) Testing was completed on a third generation device for the segmental replacement of the trachea. This device was constructed of a polylactic-polyglycolic acid shell with polyvinyl chloride coated spring steel inserted in the shell to maintain patency. These prostheses as well as others of different design and construction which were previously reported have not been successful when implanted in dogs. This particular effort has been terminated. Additional devices planned for design and construction are being done under contract and will be evaluated in-house. These evaluations will be reported under DA Accession OH 6037 and OK 6020 in FY 83.							

PROJECT: 3S162775A825

WORK UNIT TITLE: DEVELOPMENT AND EVALUATION OF METHODS AND MATERIALS FOR
TREATING TRAUMATIC INJURY

PRINCIPAL
INVESTIGATOR: COL A. F. TORTORELLI, DC

Design and Construction of Prostheses

For the Reconstruction of the Trachea in Dogs

PROBLEM: Approximately 15% of all combat injuries are of the head and neck. A significant portion of these wounds will be avulsive. The development of materials and techniques to treat these wounds at the combat surgical hospital level will result in a decrease in mortality and morbidity of combat casualties. The trachea presents a particularly challenging problem in devising a prosthesis for its replacement which will be inert, nonantigenic, allow no leaks, be rigid laterally but elastic anteroposteriorly, have a noncollapsible lumen, and allow good fixation.

APPROACH: Several devices were constructed which had in common a shell of biodegradable polylactic and/or polyglycolic acid. In order to provide for the required rigidity, nondegradable frameworks were constructed of either ceramic rings, a Teflon scaffolding, or a polyvinyl coated spring steel coil. It was postulated that the biodegradable polymers would be slowly replaced by host tissue and inclose the nondegradable frame work.

RESULTS: Each prosthesis used as its basic unit a cylinder constructed of layers alternating between PLA polymer alone and mixtures of PLA-PGA copolymer. The cylinders were prepared by spraying 10% solutions of the various polymer mixtures in methylene chloride onto a rotating mandrel of appropriate dimensions. The resulting fibrous polymer cylinders were used as inner cores slipped inside each of the three nondegradable systems used for the different prostheses (ceramic rings, Teflon scaffold, polyvinyl coated spring steel). With the inner core in place inside the nondegradable system, a final outer core of polymer was placed on each device by continuing the polymer spraying procedure until the device had a wall thickness of 0.4cm. The final prostheses were 5cm long with an inside diameter of 1.8cm. The ceramic rings used were constructed of alumina. The Teflon scaffold was constructed as a crib or partial cylinder in which the circumferential rings of the device did not meet. The spring steel was composed of medical grade stainless steel. All the devices were sterilized by megadose gamma irradiation. The Teflon scaffolding was noticeably embrittled by the sterilization process. Ethylene oxide sterilization of the Teflon containing device caused separation of the Teflon from the polymer. The polymer shells may have also been affected to some extent by the gamma irradiation. All the devices constructed and subsequently implanted in dogs failed within 6 weeks of placement.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ⁶	2. DATE OF SUMMARY ⁷	REPORT CONTROL SYMBOL DD-DR&E(AR)636	
3. DATE PREV SUMMARY 81 10 01	4. KIND OF SUMMARY D. CHANGE	5. SUMMARY SCTY ⁸ U	6. WORK SECURITY ⁹ U	7. REGRADING ¹⁰	8A. DISEM INSTR ¹¹ NL	8B. SPECIFIC DATA - CONTRACTOR ACCESS <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	9. LEVEL OF SUM A. WORK UNIT
10. NO./CODES ¹²	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
a. PRIMARY	62775A	3SI62775A825		AA		004	
b. CONTRIBUTING	62775A	3SI62775A825		AD		004	
c. CONTRIBUTING	//////////	STOG 80-7.2:5					
11. TITLE (Precede with Security Classification Code) ¹³ (U) Natural History of Oral Lesions Encountered in the Soldier							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ¹⁴ 012900 Physiology							
13. START DATE 69 07		14. ESTIMATED COMPLETION DATE CONT		15. FUNDING AGENCY DA		16. PERFORMANCE METHOD C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE:				PRECEDING		b. FUNDS (in thousands)	
b. NUMBER ¹⁵ :				FISCAL		82	
c. TYPE:				YEAR		0.5	
d. KIND OF AWARD:				CURRENT		27	
e. AMOUNT:				83		0.7	
f. CUM. AMT.						59	
20. RESPONSIBLE DOD ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME ¹⁶ USA Institute of Dental Research				NAME ¹⁶ USA Institute of Dental Research			
ADDRESS ¹⁶ Washington, DC 20012				ADDRESS ¹⁶ Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic institution)			
NAME: Sweeney, T.P.				NAME ¹⁷ Carpenter, W.M.			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3080			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
22. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Burnett, P.			
				NAME:			
23. KEYWORDS (Precede EACH with Security Classification Code) (U) Aphthous Stomatitis; (U) Wound Healing; (U) Recurrent Aphthous Stomatitis; (U) Lymphocytes; (U) Laboratory Animal							
24. TECHNICAL OBJECTIVE, 25. APPROACH, 26. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)							
<p>23. (U) To recognize, characterize and develop effective therapeutic measures for those lesions and conditions which affect the soldier due to military duty. The recognition of environmental and other factors which participate in the etiology of lesions and conditions unique to the military or are casually related to military duty will enable the development of interceptive or therapeutic measures.</p> <p>24. (U) To detect through clinical and/or microscopic observation oral lesions or a condition unique to the military population. To identify oral lesions or conditions which, though not unique to the soldier, are etiologically related to the performance of duty. Once identified the natural history including etiology, therapy, and prognosis will be established utilizing appropriate methods such as surveys, animal, and human investigations.</p> <p>25. (U) (81 10 - 82 10) Idiopathic recurrent aphthous stomatitis (RAS) appears to be a significantly greater problem in military as opposed to civilian populations and has a negative impact on the healing of oral wounds. The involvement of immune serum and/or lymphocytes as possible mechanisms in the cytolysis of oral epithelial cells is being evaluated by a radioisotope release assay using ⁵¹Cr. Results obtained to date suggest that blood mononuclear cells participate in the lysis of autologous oral epithelial cells and is dependent on the presence of heat-stable factor(s) in the serum of RAS-prone individuals.</p>							

* Available to contractors upon author's approval.

PROJECT: 3S162775A825

WORK UNIT TITLE: NATURAL HISTORY OF ORAL LESIONS

PRINCIPAL

INVESTIGATOR: LTC PAUL R. BURNETT, DC

In Vitro Correlate of Recurrent Aphthous Stomatitis:

Evaluation of Immune Cytotoxicity by Radioisotope Release

PROBLEM: Studies show that the military loses approximately one million man-hours per year to morbidity associated with maxillofacial injuries. Individuals prone to idiopathic recurrent oral ulceration or recurrent aphthous stomatitis (RAS), a group commonly believed to comprise a significantly greater proportion of the military than of the general population, manifest variably prolonged healing of oral wounds ranging from a few days to several weeks. The objective of this research is to help reduce the impact of oral and maxillofacial wounds on military manpower by elucidating the pathophysiological mechanisms responsible for the amplification of inflammation, destruction of tissue, and accompanying prolongation of healing associated with RAS.

APPROACH: A radioisotope (^{51}Cr)-release assay is being developed to quantify cytolysis within suspensions of nonkeratinizing oral epithelial cells. Using blood components from paired RAS-prone and RAS-free subjects, the four possible combinations of heat-inactivated serum with mononuclear leukocytes are assayed for their ability to lyse radiolabelled, autologous oral epithelial cells in order to evaluate the involvement of immune serum and/or lymphocytes in this lytic process.

RESULTS: Results have been modest to this point, largely due to difficulties experienced in obtaining adequate quantities of isolated oral epithelial cells by trypsinization. The variability in cell yields has been found to correlate with the supplier-determined removal times for the various lots of trypsin we have used. Best results have been obtained with enzyme lots having recorded removal times of less than 10 minutes. Trypsinized oral epithelial cells incorporated ^{51}Cr reasonably well; but the spontaneous release of the radioisotope has been somewhat greater than optimal. Preliminary data suggest that in our in vitro model, the participation of blood mononuclear cells in the lysis of autologous oral epithelial cells is dependent on the presence of a heat-stable factor(s) in the serum of RAS-prone individuals.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)636	
3. DATE PREV SUMMARY 81 10 01	4. KIND OF SUMMARY D. CHANGE	5. SUMMARY SCY ^a U	6. WORK SECURITY ^a U	7. REGRADING ^a	8. DISSEM INSTR ^a NL	9. SPECIFIC DATA - CONTRACTOR ACCESS <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
10. NO./CODES ^a		PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER		
a. PRIMARY		62775A	3SI62775A825	AA	007		
b. CONTRIBUTING							
c. CONTRIBUTING		//////////	STOG 80-7.2:5				
11. TITLE (Precede with Security Classification Code) ^a (U) New and Improved Techniques for Grafts and Bone Regeneration in Traumatic Wounds							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a 012900 Physiology 002400 Bioengineering							
13. START DATE 69 01		14. ESTIMATED COMPLETION DATE CONT		15. FUNDING AGENCY DA		16. PERFORMANCE METHOD C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE:				PRECEDING		b. FUNDS (in thousands)	
b. NUMBER: ^a				FISCAL YEAR		c. FUNDS (in thousands)	
c. TYPE:				CURRENT		d. FUNDS (in thousands)	
d. KIND OF AWARD:				83		110	
19. RESPONSIBLE DOD ORGANIZATION				20. PERFORMING ORGANIZATION			
NAME: ^a USA Institute of Dental Research				NAME: ^a USA Institute of Dental Research			
ADDRESS: ^a Washington, DC 20012				ADDRESS: ^a Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P.				NAME: ^a Tortorelli, A.			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3764			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
21. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Woodyard, S.			
				NAME: O'Neal, R.			
22. KEYWORDS (Precede EACH with Security Classification Code) (U) Tricalcium Phosphate; (U) Ceramic Block; (U) Segmental Mandibular Defects; (U) Granular Tricalcium Phosphate; (U) Laboratory Animals							
23. (U) Current methodologies for managing combat maxillofacial wounds and preventing/treating dental emergencies in the field will be extremely difficult to apply under the conditions anticipated in future war. New methods are required which will permit more rapid definitive care, reduce morbidity and decrease logistic load. Thus the objective of this work unit is to develop simple, rapid methods for soft tissue or bone grafting utilizable by the dental specialist in the field.							
24. (U) The fate, metabolism, osteogenic potential and tissue compatibility of ceramic and copolymer materials will be studied alone and in combination. The application of these and other materials to avulsive type wounds in both animals and humans will be pursued.							
25. (U) (81 10 - 82 10) Long-term evaluation (12-24 months) of biodegradable α -tricalcium phosphate (TCP) ceramic blocks for the segmental replacement of mandibular bone has been completed. Although biodegradation of and bone ingrowth into the ceramic is improved by the presence of unidirectional porosities in the ceramic, the process is very slow. Approximately one to two-thirds of the ceramic remains at 24 months post-placement. Healing is good but further improvements in ceramic designs are needed and are being constructed. The use of granular TCP to treat bone defects around teeth has been completed. It is concluded that with good post-operative care the defects can be resolved and tooth stability improved. Experiments are in progress to determine the efficacy of TCP in stabilizing tooth implants in the presence and absence of trauma.							

^aAvailable to contractors upon originator's approval.

PROJECT: 3S162775A825

WORK UNIT TITLE: NEW AND IMPROVED TECHNIQUES FOR GRAFTS AND BONE
REGENERATION IN TRAUMATIC WOUNDS

PRINCIPAL
INVESTIGATOR: COL A. F. TORTORELLI, DC

Tricalcium Phosphate Blocks in the Treatment of
Mandibular Discontinuities

PROBLEM: The loss of bone is a common sequelae of combat trauma. The use of autogenous bone where possible is a proven approach to resolving such defects. However, the extent of bone loss often makes this approach impractical and the increased chance of morbidity due to the removal of autogenous bone is a negative factor to be dealt with. The availability of an off-the-shelf material which is plentiful, storage-stable, nontoxic and biodegradable could provide a means of filling bone defects which would ultimately be resolved as new bone. Tricalcium phosphate ceramic has been studied as a bone replacement material and found to be non-toxic and have an excellent shelf-life. However, it was found to biodegrade very slowly with a tendency to crumble at a given point in time rather than maintain its integrity until completely replaced by bone. The block ceramic was redesigned to include long unidirectional channels in the expectation that this would improve bone ingrowth and biodegradation properties in-vivo.

APPROACH: Ceramic blocks were used to replace surgically removed segments in the mandibles of dogs. The blocks were placed in the discontinuities in such fashion as to align the unidirectional channels (Approximately 300 microns in diameter) parallel to the long axis of the mandible. Animals were killed at intervals of 2,6,8,12 and 24 weeks and the tissues examined histologically for bone ingrowth. Long-term animals were maintained for 24 months.

RESULTS: Previously reported results (Annual Report 1981) indicated complete ingrowth of bone into the unidirectional channels at 24 weeks post-operative with only slight biodegradation of the ceramic. Remaining animals have thus far been maintained for 24 months. Radiographic evaluation and sacrifice of one animal indicates that between 33 to 66% of the ceramic remains 24 months post-operative. However, the remaining material does not demonstrate the catastrophic fragmentation previously noted using ceramic blocks without unidirectional porosity. While the results are promising, it is concluded that the slow biodegradation rate is not conducive to a timely and uneventful resolution of bone defects. Efforts are continuing to design a material with a more rapid degradation rate.

PROJECT: 3S162775A825

WORK UNIT TITLE: NEW AND IMPROVED TECHNIQUES FOR GRAFTS AND BONE
REGENERATION IN TRAUMATIC WOUNDS

PRINCIPAL
INVESTIGATOR: COL STEPHEN G. WOODYARD, DC

Biodegradable Ceramic Powder in Human Periodontal Defects

PROBLEM: The resolution of serious periodontal defects is possible only with prolonged treatment. The accessibility of the periodontal defect to oral microorganisms and the pocket configuration of the lesion site militate against its ready resolution. The filling of these defects with autogenous bone has been demonstrated effective in resolving them. However, the increased opportunity for morbidity provided by the harvesting of autogenous bone make this approach questionable. A material which could in some way stimulate or precipitate osteogenesis and be available off-the-shelf could considerably reduce treatment time and provide a more effective modality for resolving periodontal defects.

APPROACH: Periodontal defects in a total of 51 individuals have been treated with tricalcium phosphate ceramic in powdered form. Re-entry and biopsy were taken at eight months post-operative and evaluated for osseous regeneration.

RESULTS: This study has been ongoing since 1974 and has been described in previous reports. The last patients were scheduled for re-entry procedures in March 1982. There were a number of difficulties. They included the failure of some patients to return for final evaluation and the absence of controls due to the necessity to treat all lesions observed rather than allow them to progress. The overall results suggest that there was a decrease in pocket depth and increase in attachment levels in the sample population. In no case were any undesirable effects noted. It is concluded that the tricalcium phosphate powder is useful in the resolution of serious periodontal defects.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL	
				DA OK 6020	82 10 01	DD-DR&E(AR)636	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY SCTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8. DOWN INSTN ^a	9. SPECIFIC DATA - CONTRACTOR ACCESS	10. LEVEL OF SUM
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
10. NO./CODES: ^a		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
A. PRIMARY		62775A		3S162775A825		AA 008	
B. CONTRIBUTING							
C. CONTRIBUTING		STOG 80-7.2:5					
11. TITLE (Proceed with Security Classification Code) ^a							
(U) Biodegradable Materials for the Treatment of Fractures and Soft Tissue Wounds in the Military Situation							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
012900 Physiology 010300 Miscellaneous Materials							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
68 01		CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
A. DATES/EFFECTIVE:				PRECEDING		B. FUNDS (In thousands)	
B. NUMBER: ^a				FISCAL YEAR		82 0.5 59	
C. TYPE:				CURRENCY		83 0.7 75	
D. KIND OF AWARD:				I. CUM. AMT.			
20. RESPONSIBLE DOD ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME: ^a USA Institute of Dental Research				NAME: ^a USA Institute of Dental Research			
ADDRESS: ^a Washington, DC 20012				ADDRESS: ^a Division of Basic Sciences Washington, DC 20012			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)			
NAME: Sweeney, T.P.				NAME: ^a Tortorelli, A.			
TELEPHONE: 202-576-3484				TELEPHONE: 202-576-3764			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
22. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Hollinger, J.			
				NAME:			
23. KEYWORDS (Proceed EACH with Security Classification Code) ^a (U) Biodegradable Copolymer; (U) Tracheal Grafts; (U) Diphosphoinositide-Lysozyme; (U) Laboratory Animals							
24. TECHNICAL OBJECTIVE, ^a 25. APPROACH, 26. PROGRESS (Provide individual paragraphs identified by number. Proceed last of each with Security Classification Code.)							
23. (U) To develop rapid and improved methods of treating combat injuries of the head and neck in the field using biodegradable materials. To develop premedicated biodegradable tissue fixation devices.							
24. (U) Biodegradable polylactic acid, polyglycolic acid and various combinations of these polymers as well as other polymers being developed will be applied in the development of surgical procedures for a variety of hard tissue, soft tissue and hollow organ injuries in animals and extended to man where appropriate.							
25. (U) (81 10 - 82 10) Studies on the segmental replacement of the trachea in 10 dogs have not been successful in spite of a number of modifications of the device used. Most recently a combination of biodegradable copolymer (lactide-co-glycolide) and coiled spring steel were constructed to produce an open cylindrical device. This device was calculated to be partially replaced by tissue ingrowth while retaining sufficient functional rigidity. All <i>in vivo</i> hollow organ studies have been terminated at this time. A study is in progress on the use of 50:50 poly-L(-)-lactide-co-glycolide containing a diphosphoinositide-lysozyme complex for the segmental replacement of mandibular bone in dogs. Necessary chemistries and presurgical preparations have been made and one implant has been inserted.							

^a Available to contractors upon originator's approval.

PROJECT: 3S162775A825

WORK UNIT TITLE: BIODEGRADABLE MATERIALS FOR THE TREATMENT OF FRACTURES
AND SOFT TISSUE WOUNDS IN THE MILITARY SITUATION

PRINCIPAL
INVESTIGATOR: COL A. F. TORTORELLI, DC

Replacement of an Excised Tracheal Segment
in Dogs Using Combination Biodegradable
and Biocompatible Prostheses

PROBLEM: Hollow organ injuries such as segmental loss of the trachea are difficult if not impossible to treat in some cases. A prosthetic replacement for the trachea would be a highly desirable means of treating segmental loss of the trachea resulting from combat wounds. Many materials have been used experimentally with varying degrees of success. To date no satisfactory prostheses for the trachea has been developed. The use of biodegradable materials in a prosthetic device offers the possibility of ultimate replacement of the biomaterial with functional host tissue. The purpose of this research effort has been to determine whether a fibrillar network of polylactic and polyglycolic acid copolymer inclosing a framework of biocompatible material would allow for ingress and replacement by host tissue with subsequent repair of the trachea.

APPROACH: Tracheal prostheses constructed with alternate layers of PLA and PLA-PGA preformed into cylinders and placed within frameworks of alumina, Teflon or spring steel coils; then sprayed with a polymer covering were used to replace 3cm segments of the trachea in 10 dogs. The animals were followed postoperatively for functional capability until the prostheses failed. Histochemical evaluations were made at sacrifice.

RESULTS: Prosthesis using a framework of ceramic rings bound together by a PLA-PGA cylinder were placed in 3 animals. A Teflon frame formed into a crib like shape rather than a cylinder and enclosed within a PLA-PGA cover was placed in 3 animals. Finally a coil of spring steel was inclosed in PLA-PGA and placed in 4 animals. The animals survived an average of 4.3 weeks with the longest survival at 5.6 weeks. In all cases advancing cyanosis and respiratory difficulties necessitated sacrifice. The prostheses using ceramic rings failed for two reasons. As the polymer biodegraded it distorted, pulling the rings together and in some cases rotating them so as to occlude the lumen. Some rings fractured and blocked the lumen. The Teflon cribs were apparently severely weakened by the method of sterilization (gamma radiation) and crumbled within four weeks. The spring steel prosthesis were the most successful. However, polymer broke away from the coils and occluded the lumen. Histological examination did reveal tissue ingrowth into the polymer as early as two weeks postoperatively. It can be concluded that dimensional instability of the polymer cylinders during biodegradation was one of the principal causes of failure for all the prosthesis.

PROJECT: 3S162775A825

WORK UNIT TITLE: BIODEGRADABLE MATERIALS FOR THE TREATMENT OF FRACTURES
AND SOFT TISSUE WOUNDS IN THE MILITARY SITUATION

PRINCIPAL
INVESTIGATOR: LTC JEFFREY O. HOLLINGER, DC

A Study to Evaluate Copolymers of PLA-PGA and

Diphosphoinositide-Lysozyme Complex for Bridging

a Surgically Prepared Bone Continuity Defect in the Mandible of Dogs

PROBLEM: Nearly 10% of all combat injuries are to the region of the head and neck. The mandible is frequently involved in these injuries. Reconstruction of discontinuity defects of the mandible is a challenging task for military oral and maxillofacial surgeons. Restoration of the continuity of the mandible is paramount for prevention of scar contracture and to obviate mandibulofacial complex collapse. A variety of implant materials have been studied to determine their effectiveness for initiating bone repair. Most of these materials have a significant drawback. The most promising substance for bone induction appears to be a biocompatible biodegradable copolymer of PLA:PGA combined with an acidic phospholipid-lysozyme complex (DPI-L).

APPROACH: Seven female dogs under endotracheal nitrous oxide-oxygen and halothane general anesthesia will have selected teeth extracted. After eight weeks, under similar anesthesia, a 2 cm segment of the mandible with its periosteum will be surgically removed. An implant block of 50:50 PLA:PGA-diphosphoinositide-lysozyme will then be fixed in the site using a stainless steel plate and screws. Dogs will be sacrificed at 28, 42, 56, 84, 120, and 168 days. At necropsy the implant site will be radiographed and clinically assessed and subsequently removed for histochemistry, total protein and hydroxyproline assay, enzyme analyses, cyclic nucleotide evaluation, and calcium to phosphate molar ratio will be determined.

RESULTS: To date one dog has been prepared for mandibular resection by extracting ipsilateral maxillary and mandibular dentition and performing an alveoloplasty. Eight weeks postoperatively a 2 cm segment of the mandible was removed and a PLA:PGA-DPI-L block was inserted in the defect. Reduction and fixation have been accomplished and the animal is in function. The remaining animals will be prepared by the same protocol.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY					1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD FORM 1498 16 16	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY ICTY ^a	6. WORK SECURITY ^a	7. REGRADING ^a	8A. DISSEM INSTR ^a	8B. SPECIFIC DATA: CONTRACTOR ACCESS		9. LEVEL OF SUM A. WORK UNIT
81 10 01	D. CHANGE	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO		
10. NO./CODES: ^a		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER
A. PRIMARY		62734A		3M162734A875		AQ		002
B. CONTRIBUTING								
C. CONTRIBUTING								
D. CONTRIBUTING								
11. TITLE (Precede with Security Classification Code) ^a								
(U) Study of Saliva as a Diagnostic Tool for Presence of Lethal Agents								
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a								
002300 Biochemistry								
13. START DATE			14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
79 10			CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS		20. FUNDS (in thousands)
A. DATES/EFFECTIVE:				EXPIRATION		PRECEDING		
B. NUMBER: ^a						FISCAL YEAR		
C. TYPE:				4. AMOUNT:		82		1.0
D. KIND OF AWARD:				F. CUM. AMT.		83		1.0
19. RESPONSIBLE DOD ORGANIZATION				20. PERFORMING ORGANIZATION				
NAME: U.S. Army Institute of Dental Research				NAME: U.S. Army Institute of Dental Research				
ADDRESS: Washington, DC 20307				ADDRESS: Washington, DC 20307				
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)				
NAME: SWEENEY, T.P.				NAME: Wynkoop, J.R.				
TELEPHONE: (202) 576-3484				TELEPHONE: (202) 576-3393				
21. GENERAL USE				SOCIAL SECURITY ACCOUNT NUMBER		POC:DA		
FIC				ASSOCIATE INVESTIGATORS				
				NAME: MILLER, R.A.				
				NAME: SETTERSTROM, J.A.				
22. KEYWORDS (Precede EACH with Security Classification Code) ^a								
(U) Salivary Amylase; (U) Nerve Agent; (U) Salivary Physiology; (U) Salivary Enzyme; (U) Laboratory Animal								
23. TECHNICAL OBJECTIVE. ^a 24. APPROACH. 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)								
<p>23. (U) To determine if saliva can be used as a diagnostic tool in evaluating the exposure of combat troops to chemical agents. To determine if constituents in saliva can be used to monitor the progress of therapy for chemical agent exposure. Develop a rapid, simplified field technique for diagnosis of chemical agent exposure in the combat soldier.</p> <p>24. (U) Changes in saliva produced by chemical agents and prophylactic antidotes will be evaluated. The particular areas of study will be enzyme, nucleotide, and protein components. Possible methodology developed will be evaluated in the field and at the hospital level.</p> <p>25. (U) (81 10 - 82 10) Work to date has suggested that variations in salivary amylase/total protein ratios may serve as the basis for a method for the diagnosis of chemical agent exposure in the field. Basal levels of several enzyme systems have been evaluated in the saliva of anesthetized Rhesus monkeys. In addition, these levels have been compared to experimental levels of the same systems following exposure to one of the chemical agents. Work is in progress to determine the effects of prophylactic pretreatment upon the salivary enzyme systems previously examined. Future work will compare enzyme levels from the current pretreatment study with levels from animals pretreated and subsequently exposed to a chemical agent.</p>								

^aAvailable to contractor upon originator's approval

PROJECT: 3M162734A875

WORK UNIT TITLE: A STUDY OF SALIVA AS A DIAGNOSTIC TOOL FOR THE PRESENCE OF LETHAL AGENTS

PRINCIPAL
INVESTIGATOR: CPT JUDSON R. WYNKOOP, DC

A Study of Saliva as a Diagnostic Tool for the
Presence of Lethal Agents

PROBLEM: The possible use of chemical warfare agents is a very real and potentially devastating aspect of modern warfare. The current method of diagnosing chemical agent intoxication is by clinical signs of anticholinesterase poisoning including increased secretions and muscle fasciculations. However, without specific prior knowledge of patient contact with chemical agents, diagnosis is tenuous. The situation is further complicated by the fact that certain prophylactic chemicals elicit signs and symptoms similar to the agents. Both situations are unacceptable. If a "dip stick" could be developed that would rapidly test salivary secretions for the effects of chemical agents, then the confusion surrounding a diagnosis of poisoning would not occur.

APPROACH: In an attempt to develop a fast, accurate diagnostic test for chemical agent poisoning, specific biochemical constituents in Rhesus saliva have been studied before and after agent intoxication. These constituents were found in parotid and extraparotid saliva specimens which were collected during anesthesia base-lines and incremental dosings of specific agent. Flow rates were measured at each of the samplings and the following tests were done on the specimens: (1) total protein, (2) amylase activity, (3) amylase zymogram, (4) lysozyme activity, (5) kallikrein activity, and (6) cyclic AMP.

RESULTS: Comparing base-line values of rhesus saliva collected under two widely used anesthetics, it is evident that each anesthetic causes a distinct secretion from the parotid glands as well as the other major salivary glands. The parotid and extraparotid flow rates for the Ketalar injected animals were significantly higher ($p < .006$ and $p < .0001$, respectively) than the flow rates of the Innovar injected animals. In general, the total protein and enzyme activities of the salivas collected from Innovar injected animals had higher values than those injected with Ketalar. The results indicate that Innovar slows the flow rate and indirectly increases the enzyme activity in the salivas. Comparing the values obtained from the Ketalar injected animals with the values obtained from the saliva of animals injected with a specific agent, it should be noted that the flow rates of the agent treated animals decreased consistently from the base-line values. The amylase/protein ratios in parotid saliva demonstrated a significant decrease with agent.

PUBLICATIONS

SUBMITTED:

1. Grover, P.S., Carpenter, W.M., and Allen, G.W.: Panographic Survey of U. S. Army Recruits: Analysis of Dental Health Status. Milit Med
2. Grover, P.S., Carpenter, W.M., and Allen, G.W.: Dental Emergencies Occurring Among U. S. Army Recruits. Milit Med
3. Grover, P.S., Carpenter, W.M., and Allen, G.W.: Predictability of Dental Emergencies by Panography. J Dent Res
4. Hollinger, J.O. and Gee, S.A.: Evaluation of the Parietal Bones in the Rat as a Specific Site for the Testing of Osteogenic Materials SHORT TITLE: A Simple Animal Model to Study Bone Implant Material. J Dent Res
5. Hollinger, J.O.: In Vivo Calcification Induced by a Proteolipid Complex (Lysozyme-Acidic Phospholipid). Biomater, Med Devices, Artif Organs
6. Hollinger, J.O.: A Preliminary Report on the Osteogenic Potential of a Biodegradable Copolymer of Polylactide:Polyglycolide (PLA:PGA). J Biomed Mater Res
7. Mader, C.: Mandibular Talon Cusp. J Am Dent Assoc
8. Finley, S.L. and Hollinger, J.O.: Separation of Alkaline Phosphatase Isoenzymes from Various Rat Tissues Using Flat-Bed Acrylamide Gel Isoelectric Focusing. J Dent Res
9. Russell, M., Lorton, L., St. Hoyme, L.E., and Snyder, A.J.: The Correlation Between Bone Loss and Tooth Malalignment. J Periodont Res
10. Vermilyea, S.G., Kuffler, M.J., and Tamura, J.J.: Observations of "Economical" Fixed Prosthodontic Alloys. Milit Med
11. Lorton, L., Peters, D.D., and Wong, M.: Testing the Sturdiness of Clinical Criteria with Different Methods of Simple Statistical Analysis. J Dent Educ
12. Grover, P.S. and Lorton, L.: A Bifid Mandibular Nerve as a Possible Cause of Anesthetic Deficiency in the Mandible. J Oral Surg
13. Stalkler, W.H. and Allen, G.W.: Bilateral Blind Epithelialized Tracts Associated with the Inferior Labial Frenum: Report of a Case. Oral Surg

14. Lorton, L. and DeNucci, D.: Pre-Cementation Stabilizing of Etch-On Fixed Prostheses. J Prosth Dent
15. Peters, D.D., Lorton, L., Mader, C.L., Augsburger, R.A., and Ingram, T.A.: Evaluation of the Effects of Utilizing Carbon Dioxide as a Pulpal Test. Part I: In Vitro Effect on Human Enamel Surface. J Endodont
16. Ingram, T. and Peters, D.D.: Evaluation of the Effects of Utilizing Carbon Dioxide as a Pulpal Test. Part II: In Vivo Effect on Canine Enamel and Pulpal Tissues. J Endodont
17. Grover, P.S. and Lorton, L.: Impaction of First Permanent Molars. A Case Report. Oral Surg
18. Shulman, J.D.: Linear Programming: A Resource Allocation Methodology for Dental Managers. J Pub Health Dent
19. Grover, P.S., Lorton, L., and Hollinger, J.: Incidence of Pain or Discomfort Following One-Visit Operative Treatment: A Review. J Prosthet Dent
20. Grover, P.S., Lorton, L., and Hollinger, J.: Incidence of Pain or Discomfort Following One-Visit Operative Treatment: A Clinical Study. J Prosthet Dent
21. Vincent, Jack W., Falkler, W.A. Jr., and Craig, J.A.: Comparison of Serological Reactions of Typed Fusobacterium nucleatum Strains with Those of Isolates from Humans, Canines, and a Macaca mulatta Monkey. J Clin Microbiol

IN PRESS

1. DiFiore, P.MN., Peters, D.D., Setterstrom, J.A., and Lorton, L.: The Antibacterial Effects of Calcium Hydroxide Apexification Pastes on Streptococcus sanguis. Oral Surg
2. Vermilyea, S.G., Kuffler, M.J., and Tamura, J.J.: Techniques for the Accurate Casting of Base-Metal Alloys. Milit Med
3. Guinn, J.W.III, Griswold, W.H., and Vermilyea, S.G.: The Effect of Cooling Rate on the Apparent Bond Strength of Porcelain-Metal Couples. J Prosthet Dent
4. Vermilyea, S.G., Tamura, J.J., and Mills, D.E.: Observations on Nickel-Free Beryllium-Free Alloys for Fixed Prostheses. J Am Dent Assoc

ARTICLES

1. Freccia, W.F., Peters, D.D., and Lorton, L.: An Evaluation of Various Permanent Restorative Materials' Effect on the Shade of Bleached Teeth. J Endodont 8:265-268, 1982.
2. Machian G.R., Peters, D.D., and Lorton, L.: The Comparative Efficiency of Four Types of Endodontic Instruments. J Endodont 8:398-402, 1982.
3. Setterstrom, J.A.: Controlled Release of Antibiotics from Biodegradable Microcapsules for Wound Infection Control. Army Science Conference Proceedings, III:215. 1982.
4. Skirvin, D.R., Vermilyea, S.G., and Brady, R.E.: Polymethylmethacrylate Reinforcement; Effect on Fatigue Failure. Milit Med 142:1037-1040, 1982.

ABSTRACTS

PRESENTED AT THE ANNUAL MEETING OF THE
AMERICAN ASSOCIATION FOR DENTAL RESEARCH
PUBLISHED IN THE JOURNAL OF DENTAL RESEARCH, SPECIAL ISSUE 61, 1982

1. Tortorelli, A.F.: Biodegradable Materials Research in the U. S. Army - A Review.
2. Setterstrom, J.A.: In Vivo Evaluation of Controlled Release Microencapsulated Antibiotics Topically Applied to Wounds.
3. Hawley, C.E.: Factors in Bone Growth and Repair: The Challenge for the Military in the Future.
4. Finley, S.L.* and Hollinger, J.O.: Separation of Alkaline Phosphatase of Rat Tissues by Isoelectric Focusing (IEF).
5. Hollinger, J.O.: The Osteogenic Potential of a 50:50 Polylactic Acid-Polyglycolic Acid (PLA:PGA) and Diphosphoinositide-Lysozyme Complex.
6. Hawley, C.E. and Heath, J.R.*: Isolation of Active Osteoclast Activating Factor (OAF) Subunits by Ultrafiltration.
7. Miller, R.A.*, Wynkoop, J.R. II, and Johannsen, K.: Analysis of Hydroxyproline in Gingival Exudate by High Performance Liquid Chromatography.
8. Wynkoop, J.R.II*, Miller, R.A., Cheong, V., and Lorton, L.: Levels of Neuroactive Substances Following Exposure to Methyl Methacrylate Monomer.

9. Wynkoop, J.R.II, Woodyard, S.*, and Miller, R.A.: A Comparison of Individual Crevicular Fluid Hycroxyproline Levels to Periodontal Assessments.
 10. Miller, R.A., Wynkoop, J.R.II, Allen, G.A.*, and Lorton, L.: Some Effects of Methyl Methacrylate Monomer Upon Renal Function.
-
11. Tortorelli, A.F.* and Grower, M.F.: Attempts at Replacement of an Excised Tracheal Segment in Dogs Using Combination Biodegradable and Biocompatible Prostheses. Proceedings of 14th International Biomaterials Symposium, Society for Biomaterials.
 12. Grover, P.S.* and Hollinger, J.O.: The Potential of a Proteolipid Complex (Lysozyme-Acidic Phospholipid) to Produce Osteogenesis. Proceedings of 14th International Biomaterials Symposium, Society for Biomaterials.
 13. Hollinger, J.O.: The Osteogenic Potential of a Complex Consisting of a Biodegradable Copolymer and Diphosphoinositide-Lysozyme. Proceedings of 14th International Biomaterials Symposium, Society for Biomaterials.

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